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Prospective Effort and Choice

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Prospective Effort and Choice

by

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I dedicate my thesis work to my late grandfather, Leo Francis Slattery (1920-2014). His passion for knowledge and lifelong encouragement to explore and question the natural world greatly inspired my pursuit of academic research.

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Prospective Effort and Choice

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The University of Texas at Austin, 2014

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We constantly face the challenge of selecting among actions in pursuit of our goals. Behavioral theories suggest the ubiquity of these choices necessitate a valuation process that integrates expected costs and outcomes. Increased sensitivity to costs in value-based choices, such as reduced willingness to tolerate risk, wait or work for rewards, features prominently in the symptomatology of mental illness. Contrary to classical theories of choice that do not distinguish among cost type, the recent unification of experimental economics, psychology and neuroscience describes the influence of specific costs upon behavioral and neural correlates of subjective value. Despite substantial progress in the understanding of the basis of subjective valuation under delay and risk, the specific influence of effort, the energetic cost of an action, remains largely unknown. Limited existing accounts hypothesize that cost sensitivity during subjective valuation results from separable neural systems related to risk, delay and effort. This dissertation evaluates evidence for distinct neural representation of effort and presents a set of experiments designed to refine normative accounts of effort-based choice. First, I review the neural basis of economic choice under risk and delay. Second, I review limited accounts economic choice under effort. I describe a novel prospective effort task designed and validated to examine effort-based valuation and address potential confounds present in previous studies. In the first experiment, I report novel evidence for discounting of neural activity related to value by prospective effort and conjoint sensitivity to effort costs and expected outcomes in brain regions related to selection and generation of actions. In a second experiment, I examined the influence of prospective effort costs upon delay discounting preferences. This experiment did not find modulation of individual preferences by prospective effort costs. Finally, I discuss our results in the context of existing accounts and potential extensions of the prospective effort paradigm. Overall, I show that prospective effort imposes a specific cost, reflected in behavioral and neural correlates of value, and presents a novel approach to further the understanding of motivated behavior.

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Chapter 1

Introduction

1.1 Thesis Summary

We often face choices between uncertain prospects associated with energetic costs. For example, consider the choice between two equally rated, unfamiliar restaurants at different distances. The value of a trip to neither restaurant is certain, but they differ substantially in potential energetic cost. Adaptive behavior requires integration of these costs and benefits to guide choice. An extensive body of work in economics and neuroscience describes the interaction of costs and benefits upon behavioral and neural correlates of subjective value. However, the specific influence and representation of effort, the energetic cost of a decision option, remains clouded by confounds and a lack of consensus. In this thesis, I describe a set of model-driven behavioral and neuroimaging experiments designed to characterize the neural representation of effort and its role in economic choice behavior.

General deficits in decision making, particularly reduced motivation to work for reward, feature prominently in the symptomatology of psychiatric disorders such as depression and schizophrenia. Characterizing the neural representation of effort and its influence upon choice behavior will provide crucial new evidence for models of normal brain function that inform the treatment of these disorders. The behavioral and neuroimaging experiments that comprise this thesis attempted to elucidate the specific influence of effort in modulation of valuation processes in choice with incentive compatible decision making tasks adapted from previously described domains, risk and intertemporal choice.

Behavioral experiments provide the basis for two sets of neuroimaging analyses that characterize the representation of effort and valuation in the brain. A set of univariate analyses extend previous analyses applied to economic choice tasks and examine the relationship between behavioral and neural correlates of sensitivity to effort costs. A second set of multivariate analyses test for similar patterns of neural activity related to effort during production and choice. In total, the experiments described herein represent the first systematic attempt separate valuation from effort production and reward receipt, a critical advance to test the representation effort-based valuation and advance normative accounts of cost-based choice.

1.2 Literature Review: The Neural Basis of Valuation

1.2.1 Abstract

Economic decision making refers to decisions that involve mainly monetary rewards between courses of action with different potential outcomes. The emergence of neuroeconomics, the integration of decision making perspectives from behavioral economics, psychology, and the neurosciences, provides a framework to link normative accounts of decision making to brain activity and behavior. To illustrate the advance of this approach, we focus on two types of economic decision making addressed by brain imaging and neuroeconomic research: decision making under risk and intertemporal choice. We present an overview of risk and economic decision making, relevant behavioral paradigms from economic and psychological research and neuroimaging results that link neural activity to specific patterns of decision making. The following text adapts a forthcoming chapter entitled *Neuroimaging of Economic Decision Making* in *Brain Mapping: An Encyclopedic Reference*, by the author and Tom Schonberg.

1.2.2 Economic decision making and Neural Correlates of Value

How the brain makes choices constitutes the primary focus of neuroeconomics, a nascent discipline that combines economic theory, choice behavior and biological measurements from the neurosciences. Much of the growth of this research followed the rise of functional magnetic resonance imaging (fMRI) in cognitive neuroscience. Functional MRI enables researchers to non-invasively observe neural activity in humans during economic decision making tasks. Foremost, these studies have established that neural activity related to the value of a chosen action occurs in several brain areas during stages of economic decision making (Rangel et al., 2008). Neural signals related to value include individual stimulus values, action/outcome values and prediction errors. However, whether these signals reflect unitary representations of value or components of other cognitive processes remains controversial (O'Doherty, 2014). Overall, neuroimaging studies complement other neural data to inform descriptive models of choice. As discussed in this chapter, this reductive approach has begun to influence our understanding of choice behavior.

1.2.3 Economic Decision Making Under Risk

Economic decisions are generally understood to occur under risk. As discussed by Schonberg et al. (2011) there exists a gap between the psychological and economic definition of risky decision making. Economists refer to risk as the variance of all possible outcomes (Markowitz, 1952). According to this definition, a risk-seeking person favors a higher variance prospect over a lower one when expected value is equal between the two options. On the other hand, psychologists as well as lay people generally refer to a risky decision as one that involves potentially incurring a loss or harm (Steinberg, 2008). These separate definitions have led to the use of separate tasks in neuroimaging studies of risky decision making. Early tasks defined risk-taking as variance of potential outcomes. These studies typically contrasted safe options with sure wins versus risky ones where the probabilities of outcomes were known. Several brain regions implicated in reward processing and value-based decision making have emerged in imaging studies involving these tasks. Regions involved in processing of risky versus safe options include the anterior cingulate cortex (ACC), insula and the dorsolateral prefrontal cortex (dlPFC) (Critchley et al., 2001; Paulus et al., 2003; Kuhnen and Knutson, 2005). One notable effort to separate reward from processing the quadratic nature of risk as variance of outcomes by Preuschoff et al. (2008) found risk-related signals in anterior insula and ventral striatum. The authors used a model-based approach to segregate changes in expected value and prediction error from encoding of the variance of potential outcomes The regions implicated in these paradigms, striatum and insula, are linked to processing of reward and aversive emotion (Tom et al., 2007; Palminteri et al., 2012), a necessary component of risky decisions. Related studies associated increased individual tendency for risk-seeking with neural activity within frontal regions implicated in reward and value processing, including orbitofrontal cortex (OFC), and ventromedial prefrontal cortex (vmPFC) (Tobler et al., 2006; Xue et al., 2009). Risk-averse behavior has been linked to increased activity in more dorsal frontal cortical areas (dlPFC, inferior frontal gyrus), regions that were previously linked to exertion of self-control (Dosenbach et al., 2006). For example, Hare et al. (2009) demonstrated that exertion of self-control in a food choice paradigm involves the modulation of value signals in vmPFC by signals within dlPFC. The contribution of attention and self-control to risk-taking behavior remains an active area of neuroimaging research.

1.2.4 Naturalistic Risk Taking Tasks

While many studies have begun to link economic measures of risk-taking behavior to neural activity, a gap remains between laboratory tasks and risky decision making in the real world (Schonberg et al., 2011). Thus, there exists a need for a set of tasks to link naturalistic measures and the typical behavioral tasks of economics and psychology laboratories. One such example (others are reviewed in Schonberg et al. (2011)) that has been extensively used for assessment of risk-taking in recent years is the Balloon Analog Risk Task (BART) (Lejuez et al., 2002). In this task, participants sequentially decide to pump or not pump a balloon that represents accumulated wealth. The size of the balloon on the screen increases with each pump. Critically, by deciding not to pump the balloon, participants 'cash-out' the wealth accumulated up to that trial. Participants know that while additional pumps increase the potential gain, they could lose all potentially accumulated wealth for that trial if too many pumps are made. Increased risk-taking (measured as average number of pumps taken in the BART) has been linked to drug use, smoking, unprotected sex and more (See Helfinstein et al. (2014) for a list of relevant studies). Neuroimaging studies of the BART, e.g. (Rao et al., 2008; Schonberg et al., 2012) found that neural activity during risk-taking occurs in dlPFC and vmPFC, the same regions found by studies that used the economic definition of risk discussed above. See figure 1.1 for details. However, these regions cannot be solely attributed to risk-taking. In the BART, each pump (additional risk-taking) conflates several factors: increasing potential gains, increasing potential losses, and increasing probability of loss and variance of potential outcomes. Consequently, although this task predicts real-world risk-taking, neuroimaging studies with the task have shown activations related to all of these factors, rather than isolated activity related to risky decision making.

Helfinstein et al. (2014) addressed this confound of earlier BART studies with a multivariate voxel-pattern classification technique. This approach attempted to equate all BART factors by testing the ability of a classifier trained upon neural activity from trials prior to the decision to pump or cash-out to predict what the participants will do on the subsequent trial. The authors found that activity within a network of brain regions related to cognitive control best predicts participants subsequent behavior in the BART. This cognitive control network, rather than regions related to increased potential reward, seems to determine if participants will take more risk in a subsequent trial. This result suggests that increased risk-seeking behavior in the real world may relate more closely to a lack of ability to adaptively inhibit responses, rather than seeking greater overall value or large individual rewards.

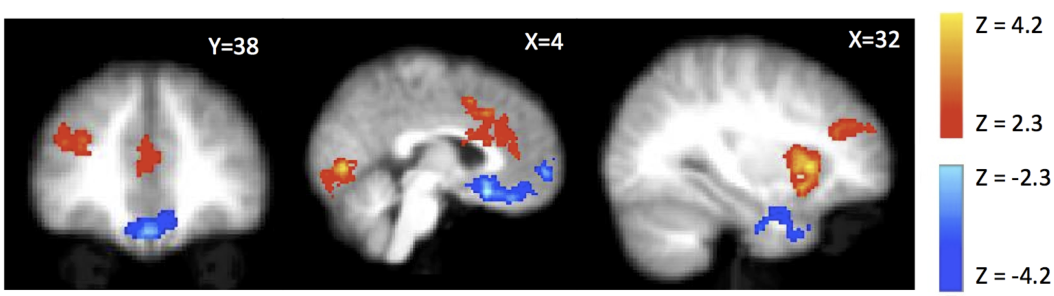

Figure 1.1: *fMRI activations related to parametric analysis of increased risk taking in the ballon analog risk task (BART). Warm colors indicate regions where neural activity positively correlated with increased risk taking behavior (ACC, insula and lateral PFC). Cool colors indicate regions that were negatively correlated with increased risk taking behavior (vmPFC and MTL). Together, these regions were sensitive to potential gains, losses and probability in the task. Figure adapted with permission from Schonberg et al., (2012)*

1.2.5 Prospect Theory and the Brain

Motivated by the failure of the prescriptions of classical economics to account for commonly observed biases in choice, Kahneman and Tversky (1979); Tversky and Kahneman (1992) developed prospect theory, the most successful normative account of choice behavior, to describe behavior under risk. For example, common behaviors such as avoidance of small risks framed as losses and reluctance to gamble with profits deviate from classical economics rational prescriptions to maximize gains. For example, snack foods labeled 99% fat free or 1% fat offer the same dietary value, but consumers' greater sensitivity to negative information (fat content) encourages advertisers use of a positive frame. Overall, prospect theory provides context for these realistic deviations from optimality with a mathematical and conceptual framework for choices under risk. Briefly, prospect theory describes choices as made from the status quo, a reference point for comparison of potential gains and losses. A value function describes the utility of gains and losses relative to the status quo (See figure 1.2). This function exhibits asymmetries that reflect loss aversion, greater decreases in value for losses compared to increases in value for equivalent gains. Additionally, prospect theory describes asymmetric sensitivity to probabilities of outcomes, characterized by a typical decision-makers tendency to weigh low probabilities related to an outcome more heavily than greater ones.

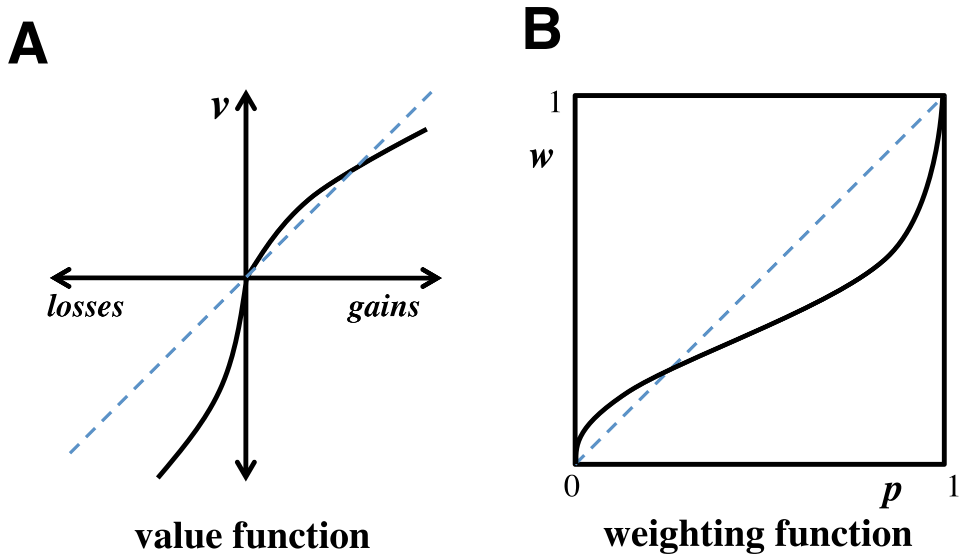

Figure 1.2: *Prospect theory describes choice behavior under risk according to nonlinear value and probability weighting functions. (A) A typical value function (v), describes the value of gains and losses relative to a decision makers reference point. The change in slope from gains to losses reflects greater change in relative value for losses over gains. (B) Nonlinear decision weight (w) function of objective probabilities (p). Curvature reflects underweighting of high probabilities and overweighting of high probabilities. Figure adapted with permission from (Schonberg et al., 2011)*

Overall, the distortions of probability and changes in value described by prospect theory suggest that economic choices reflect these biases and other rules employed to simplify them, rather than representation of a vast set of complex outcome expectations. Accordingly, neuroimaging provides an opportunity to examine the relationship between behavior under risk and brain activity related to value to test the predictions of prospect theory. Tom et al. (2007) examined neural activity with fMRI while participants completed a task to assess loss aversion behavior, the mixed gambles paradigm. During this task, subjects chose to accept or reject lottery tickets that offered an equal chance at winning or losing varied amounts of money. The authors found that within vmPFC and striatum, patterns of neural activity followed the asymmetric pattern of greater sensitivity to potential losses over gains predicted by prospect theory. Additionally, individual differences in subjects sensitivity to losses as compared to gains also reflected individual differences in neural activation within the same network of brain regions (See Figure 1.3).

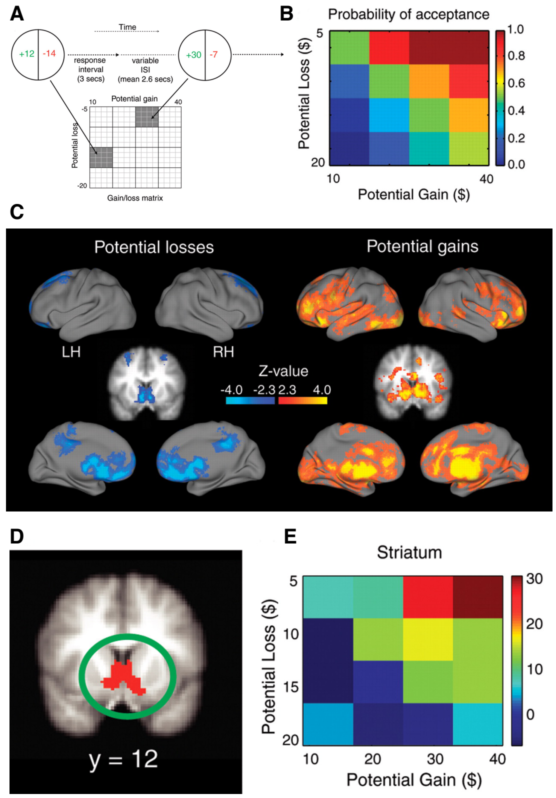

Figure 1.3: *The neural basis of loss aversion: (a) Illustration of the event-related mixed-gambles task design. During each trial, participants accepted or rejected prospective mixed-gambles (equal probability of gain or loss). (b) Heatmap of probability of gamble acceptance at collapsed levels of gain and loss. Warmer color indicates greater willingness to accept a gamble. (c) Whole-brain parametric responses to the size of potential loss (cool colors, left) or gain (warm colors, right). Gain sensitive regions include vmPFC, striatum, cingulate cortex and dopaminergic midbrain regions. Loss sensitive regions also included vmPFC, cingulate cortex and striatum. A conjunction analyses demonstrated joint sensitivity to gains and losses in vmPFC and striatum. (d) Map of striatum region (red pixels) with joint sensitivity to gain and loss, and heatmap (e) of cluster within green circle (d). Heatmaps average parameter estimates versus baseline within cluster for each of 16 cells of gain/loss matrix. Color-coding indicates strength of neural response for each condition, illustrating greatest activation (warm color) and deactivation (cool color). These results show asymmetric activation for gains and losses within the same valuation region, related to choice behavior described by prospect theory in (b). Figure adapted with permission from Tom et al., (2007).*

Controversially, neural activity within regions previously implicated in the experience of pain or loss, such as the insular cortex and amygdala, did not exhibit a pattern related to loss aversion. However, subsequent studies demonstrated involvement of these regions in closely related tasks (De Martino et al., 2010; Canessa et al., 2013). These results support a proposal that neural activity patterns related to loss aversion result from the modulation of vmPFC and striatal activity by affective processing regions such as amygdala and insular cortex, , rather than single valuation process within them. The precise causal role of regions outside of the core valuation network remains an active area of research. To examine neural activity related to the framing effect, De Martino et al. (2010) presented subjects with a choice between sure outcomes and gambles, each equivalent in expected value, in either gain or loss frames. Acceptance of a sure gain in the gain frame or risky loss in a loss frame evoked amygdala activity, consistent with the proposal that framing effects result from hedonic processes related to aversion. Activity in regions related to cognitive control, such as anterior cingulate cortex and dorsolateral prefrontal cortex increased when the opposite choices occurred. As demonstrated with loss aversion (Tom et al., 2007) and nonlinear probability weighting (Hsu et al., 2009) the authors found that neural activity in striatum related to individual changes in choice. Together, these studies have begun to identify the neural correlates of prospect theory, the interaction of a core valuation network with networks of regions related to emotional drives and cognitive control. The causal role of activity within the core valuation regions and those linked to affective distortions of value remains a major focus of neuroeconomics.

1.2.6 Intertemporal Choice

Economic decision makers often face intertemporal choices, decisions that differ in the timing of their outcomes. From an individual choice between renting or buying, to a governments' investment in environmental protection, these choices require consideration of what an outcome is worth to the decision-maker in the future. Therefore, the ability to evaluate the future consequences of a choice necessarily requires the integration of what an outcome is worth and its associated delay. Studies of intertemporal choice focus upon the robust finding that humans and animals exhibit delay-discounting behavior, choice preferences that suggest equivalent rewards become less valuable in the future as compared to the present (Kirby and Herrnstein, 1995; Kim et al., 2008). Behavioral models of choice describe the value of a reward outcome available later in time according to a discount function, the form of which characterizes how the value decreases over time. To estimate this function, studies typically present subjects with a series of choices between small rewards available immediately and larger rewards of varying size available at one of several later times. Notably, choices in human and animal studies may differ in important ways. Early human studies often presented hypothetical choices, while animal studies necessarily presented actual delays to consumable rewards after each choice. In an attempt to address the ecological validity necessary to compare findings across species, more recent human studies select a single trial at random from the experimental session, and honor the subjects choice accordingly. In either case, a discount function estimated from intertemporal choices, compared to the fit of a decay function, characterizes the rate at which an individual animal or human subject devalues rewards over time.

The preferred form of the discount function employed in studies of intertemporal choice reflects the evolution of the study of these choices and remains a source of debate. Theoretical work on intertemporal choice in economics historically focused on prescriptions of how decision makers should discount the value of delayed rewards. The exponential discount model, based on the work of Samuelson (1937), presented the first widely accepted account of discounting over time. Despite the simplicity and success of this model, advanced over several decades, converging evidence now suggests humans and animal behaviors do not truly reflect the assumptions of exponential discounting. For example, Mazur's (1987) study of intertemporal choice in pigeons concluded that their behavior fit more closely to a hyperbolic discount function. This characterization allows the weight of discounting to vary over time, rather than the fixed decay of exponential discounting. Hyperbolic or quasi-hyperbolic discount rates provide a superior fit to human and animal behavior over exponential decay models in studies of delayed reward and punishment alike, in monetary and non-monetary domains. Consequently, neuroimaging studies of intertemporal choice now focus on these discount forms. An important debate within the study of intertemporal choice centers upon how hyperbolic preferences might arise. Broadly, theoretical accounts in psychology and economics emphasize a competition between rationally deliberate and irrationally emotional processes (Ainslie, 1975; Loewenstein, 1996). These views comprise a dual-process account that links the observation of hyperbolic discounting to the competition of a system that strongly favors immediate rewards with a second that more rationally values rewards across time (Loewenstein and O'Donoghue, 2004). Similar normative accounts of competition between 'hot' and 'cold' systems during choice follow this model, whereby failure to suppress the 'hot' system results in suboptimal bias for immediate rewards (Metcalfe and Mischel, 1999). Formally, dual process models fit quasi-hyperbolic or beta-delta discount functions to choice behavior, whereby two parameters reflect the separate influence of patient and impulsive systems (Laibson, 1997). Alternatively, single-process models posit a unitary discount process akin to a general hyperbolic function fit by a single parameter (Kirby, 1997). See Figure 1.4 for examples of typical temporal discount functions. Given the relevance of understanding the neural mechanisms of intertemporal choice to major public health issues, many neuroeconomic studies attempt to link behavioral preferences to specific neural correlates. As in studies of choice under risk, these studies also provide evidence for a core network of brain regions for valuation.

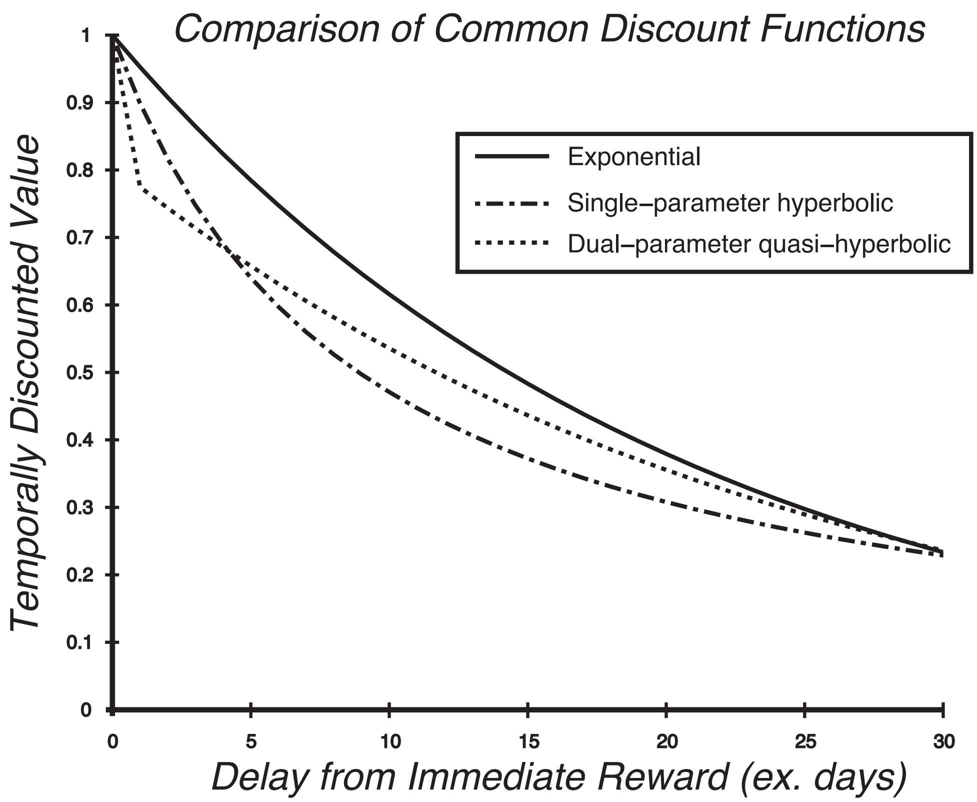

Figure 1.4: *Examples of typical temporal discount functions: Exponential discounting assumes a constant rate of discounting, e.g. δ (t) where δ is the discount rate (here, δ =0.96). Hyperbolic discounting is generally greater for short time periods than long periods, and can be described by a function of the form 1/(k * t + 1), (here, k = 0.11). Quasi-hyperbolic discounting is a piecewise function that follows a form similar to exponential discounting after the first discount period (i.e. the first day): (Here, β = 0.8 and δ = 0.96.) Figure adapted with permission from (Berns et al., 2007).*

1.2.7 Functional Neuroimaging Evidence for Temporally Discounted Value

The recent work of two groups summarizes attempts to resolve the neural mechanisms that contribute to intertemporal choice behavior. A series of studies by McClure et al. (2004, 2007) support a dual-process model of discounting. In their first study, subjects made a series of choices between pairs of hypothetical rewards. Their analyses split trials into two types. In the first type, both rewards were available at some point in the future. The second type always offered an immediate, smaller reward. Comparison of these trials found one set of brain regions (vmPFC, cingulate cortex, striatum) more active during choices with immediate rewards than delayed rewards only. Activity in lateral prefrontal and intraparietal regions increased compared to baseline during rest and increased reaction time. By comparing the activity of these two systems during trials with an immediate reward, the authors successfully predicted choice behavior. They argued these results reflect the competition of brain regions that comprise the patient and impatient systems predicted by dual-process theory. In their interpretation, neural activity in the medial prefrontal cortex and striatum constitute the impatient *beta* system, while the limbic and lateral prefrontal cortex constitute the more patient *delta* system. A replication of this study with primary rewards (juice available to thirsty subjects) and shorter delays (up to twenty minutes) supported the initial finding, and again enabled prediction of choice by comparison of activity in these two defined networks of brain regions (McClure et al., 2007).

While these results support the conception of delay discounting as a competition between structures related to evolutionarily older, irrational drives and more evolved, rational deliberation, two subsequent studies by a second group of authors, Kable and Glimcher (2007, 2010), argued for an alternative, single-process interpretation. Unlike the previous studies, the authors estimated the value of the discount rate for each subject, following Mazur's (1987) single-parameter hyperbolic formula. Subjects' discount parameters allowed them to compare fMRI activity to predicted value, which elicited a network of regions related to the subjective value of delayed reward options. They found that while some of these regions overlap with the *beta* system of the dual-process model (vmPFC, posterior cingulate cortex, striatum) neural activity within these regions did not exclusively increase to immediate reward. Importantly, these results suggest that activity in these regions during choice evaluation reflects a unified representation of discounted subjective value within a core valuation network, rather than fully separable discounting processes. Kable and Glimcher's second study compared the two trial types of McClure and colleagues original study (Kable and Glimcher, 2010). Again, choices that presented two delayed options were compared to choices with one immediate reward and one delayed reward. Neural activity in McClure et al.'s *beta* system regions again reflected estimated subjective value, regardless which reward type was more valuable. More recent studies provide additional evidence for neural activity related to components of valuation within core valuation regions during intertemporal choices. For example, two studies link activity within striatum at choice to magnitude of delayed rewards (Pine et al., 2009) and differences in discounting behavior (Hariri et al., 2006). Figure 1.5 summarizes brain regions related to aspects of intertemporal choice. Like economic decisions under risk, further understanding of the neural basis of intertemporal choice will require investigation of how regions that demonstrate discounted value representations reported thus far interact with brain networks related to other processes, particularly emotion, self-control and memory.

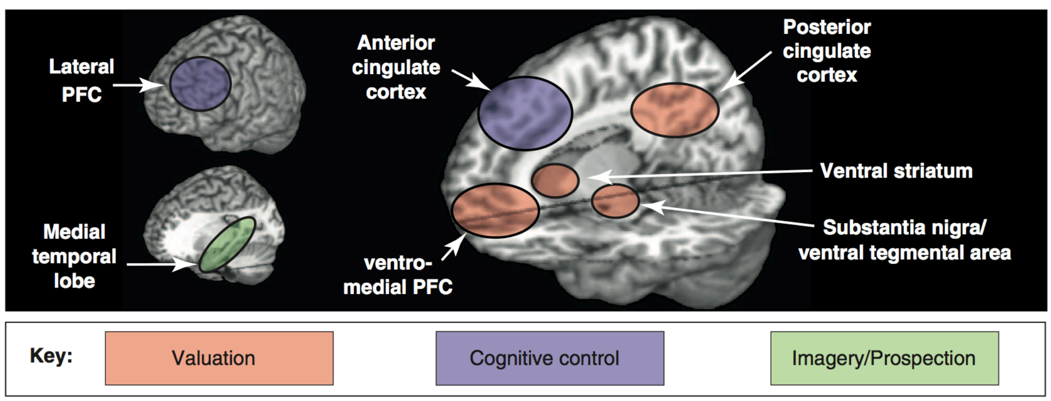

Figure 1.5: *Several brain networks have been implicated in economic decision making in the realms of intertemporal choice and risky decisions: the valuation network includes the vmPFC, striatum and dopaminergic midbrain areas. The cognitive control network, involved in modulation of risk-taking behavior, includes lateral frontal regions and cingulate cortex. Figure adapted with permission from (Peters and Büchel, 2011).*

1.3 Discussion

Neuroimaging research has contributed important evidence in support of neuroeconomics' goal of a unified economic decision making model. This chapter reviewed the key contribution of neuroimaging to this endeavor, identification of neural correlates of predictions of valuation from economic theory. In the area of risky decision making we first reviewed recent studies that extend our understanding of the link between a classical economic definition of risk and risky decision making in everyday life. These studies have begun to unify assessment of risk-taking in the neuroimaging laboratory with measurements of risky behavior in the real world. As discussed, the interaction of a network of brain regions related to cognitive control and a core valuation network contribute to observed risk-taking behavior. Second, we discussed efforts to test the predictions of prospect theory, the leading model of decision making under risk, with neuroimaging data. Several studies have identified changes of value related neural activity during decision making under risk that reflect loss aversion, asymmetric weighting of probabilities and reference dependence, central predictions of prospect theory. Finally, we reviewed leading theories of intertemporal choice behavior and their neural correlates. While initial studies supported a dual process model of competing neural systems with different sensitivity to delay, converging evidence points to a unified representation of discounted value within a core valuation network.

While these advances and the contributions of related studies support continued neuroimaging studies of economic decision making, the field faces several challenges to inform the broader understanding of human behavior. The rise of pattern classification techniques has shifted neuroimaging research away from contrasting patterns of activity to understanding the representation of information. Applied to economic decision making, these techniques could attempt to predict choice from patterns of neural activity. Studies have begun to reveal information representation within a core valuation network, e.g. (McNamee et al., 2013), but reliable prediction of economic choice will require clever task design and analyses to isolate relevant neural signals (O'Doherty, 2014). Finally, neuroimaging data have provided crucial evidence to test theoretical accounts of economic decision making, but they have been slower to contribute to refinement of economic theory. Further interdisciplinary work is needed to advance normative accounts grounded in economic theory and constrained by their biological substrate. In the proceeding chapters, I present a set of experiments designed to test the role of physical effort, a specific, ethologically valid decision cost, in economic decision making under risk and delay.

Chapter 2

A Novel Task to Examine Effort-Based Choices

2.1 Chapter Summary

This chapter provides an introduction to the behavioral paradigm and models used throughout the experiments described thereafter. First, I describe behavioral paradigms previously employed to assay effort-based valuation and identify critical features that motivated the development of the prospective effort paradigms used herein. I describe the core elements of the prospective effort paradigm and present the results of three pilot studies designed to validate it. With the paradigm established, Chapters 3 and 4 present experimental work that evaluates effort-based decision making in the context of economic choices under risk and delay.

2.2 Introduction

Effort is generally considered to decrease the value of an action. Adaptive organisms readily exert effort to achieve goals, but attempt to minimize effort in doing so. Many behavioral experiments demonstrate discounting of reward by effort in response rates to monetary and food rewards (Walton et al., 2006; Kool et al., 2010). In these studies, human and animal subjects demonstrate reduced behavioral and neural signatures of value as the effort required to achieve a reward increases. Valuation of rewards and costs are well studied individually, but the understanding of their integration with effort remains limited by a small number of accounts with often conflicting results. I developed a novel approach to isolate and test the role of effort in establishing subjective value from of a mixture of potential costs and rewards. First, I review pertinent reports of reward and effort integration in the decision- making literature, with a particular focus upon the involvement of dopamine (DA) and norepinephrine (NE) systems and conclude with open questions addressed by this proposal. The literature emphasizes these neuromodulatory systems and a network of cortical and basal ganglia regions as the principal components of a network that represents and integrates information about costs and benefits to guide actions.

2.2.1 Valuation and the Dopamine in the Brain

Current theories of decision making propose an interaction of multiple brain systems, with specialized circuits for representation and integration of variables in sequential stages of an evolving choice (Rangel et al., 2008; Padoa-Schioppa and Cai, 2011). The fundamental stages include representation of possible actions and states, valuation of actions, action selection and outcome evaluation for learning and memory. Leading theories of the neural representation of reward implicate the mesolimbic dopaminergic system and its projections to prefrontal cortex in the motivation of effortful behavior (Salamone and Correa, 2012). Theories concerning dopaminergic function have evolved considerably since the initial link of dopamine to reward. Briefly, study of the dopaminergic system initially suggested a general role in reward and hedonic value, but evolved to include learning through prediction errors, approach behavior, vigor control and salience (Wise, 2004). Two findings regarding the proposed role of dopamine in overcoming effort costs and controlling response rate are of particular interest for our proposal. Several studies demonstrate that depletion of dopamine in the nucleus accumbens disrupts instrumental responding if a high effort is required, but not if effort required is minimal (Salamone et al., 2007). A review of this research proposed that tonic dopamine levels in striatum reflect the average rate of reward in the environment, an important variable for an organism to infer benefits and control response behavior (Niv, 2007). Diverse neuroimaging studies place representation of value in a network of dopamine associated prefrontal and basal ganglia regions, centered upon the ventromedial prefrontal cortex and ventral striatum, supported by complimentary findings from single neuron recordings in animals (Knutson, 2005). These studies suggest functional specialization of reward processing, with accumbens encoding dopaminergic reward prediction errors, and ventromedial frontal cortex encoding a general abstract reward value that guides choice (Rangel and Hare, 2010; Lee, 2013).

2.2.2 Neural Correlates of Valuation Processes

Neural correlates of processing loss and risk are less well defined than reward, but studies commonly implicate the anterior insula, amygdala and cingulate cortex with these costs (Liu et al., 2011; Palminteri et al., 2012). Similarly, many reports describe different interactions between costs and benefits in choice, including risk, probability, delay, and pain (Tom et al., 2007; Pessiglione et al., 2007; Kable and Glimcher, 2007; Talmi et al., 2009). Generally, these studies report modulation of value signals in cortical areas that reflect an integration of these costs with reward. These studies suggest several cortical areas as potential integrators of costs and benefits, including orbitofrontal cortex, lateral prefrontal cortex and anterior cingulate cortex (Rangel and Hare, 2010; Walton et al., 2007; Rogier B Mars and Yeung, 2011). Together with studies of valuation, these studies highlight a network of regions implicated in integration of certain costs and benefits in choice, critical for understanding the distinct role of effort in similar choices. Similarly, a growing body of work in the noradrenergic system encourages consideration of neurotransmitters beyond dopamine upon choice. Anatomical connectivity and experimental evidence supports an interplay between the norepinephrine and dopamine systems in decision making. For example, theoretical and experimental work suggest reciprocal projections between cingulate cortex and the brainstem nucleus locus coeruleus enable flexible control of broad attentional resources (Aston-Jones and Cohen, 2005; Sara, 2009). While accessing brainstem dopamine and norepinephrine activity remains difficult with neuroimaging, the revival of pupillometry provides an approach to infer activity in these regions (Nassar et al., 2012).

2.2.3 Previous Effort-Based Neuroimaging Studies

Several recent human neuroimaging studies address the role of effort in selecting an action and inform the experiments proposed here. Croxson and colleagues investigated the location of blood oxygenation level dependent (BOLD) signals associated with the subjective value of stimuli that represented mixtures of monetary rewards and the number of movements required to earn them, increasing cost in terms of both effort and time (Croxson et al., 2009). In the absence of a choice, the authors found striatum activity correlated with increasing reward and effort requirements. Another study similarly reported higher striatal activity for choosing low effort over high effort, consistent with effort discounting value (Kurniawan et al., 2010). A notable study that offered forced choices between high or low efforts paired with high or low rewards also found striatum to represent effort and delay-discounted reward and further reported the integrated representation of effort and reward in the dorsal ACC (Prevost et al., 2010). This study reported a negative interaction in ACC, whereby increased activity reflects prospects that are more effortful, subjectively less valuable. This result is consistent with a role for ACC in effort previously shown in animal lesion studies. For example, a series of studies in animals report damage to ACC but not OFC biases animals to select low-effort options when a more rewarding high-effort option is available (Rudebeck and

Murray, 2011). Single neuron studies implicate ACC in effort discounting of reward as well, observing that ACC neurons increase their activity as monkeys face increasing action steps to reward (Shidara, 2002). A few studies also implicate orbitofrontal cortex (OFC) as an integrator of costs and efforts in choice or report modulation of activity at the level of motor effectors in effort tasks (Gershman et al., 2009; Wunderlich et al., 2009; Burke et al., 2013). While this literature suggests effort contributes to decision related activity, the dynamics of ongoing effort-based choices in humans remain largely unexamined. A recent study suggests the decision to invest or withhold physical effort relates to accumulating cost evidence in a proprioceptive region, the posterior insula, consistent with an accumulator model previously demonstrated to account for neural activity when considering monetary gains and losses alone (Basten et al., 2010; Meyniel et al., 2013). In summary, these studies demonstrate that effort-based decisions modulate prefrontal-striatal neural circuitry implicated in valuation of options. However, no study to date has systematically isolated the behavioral and neural representation of effort as a cost and compared it to other common costs in value-based decisions. To fully understand the establishment of action value from mixtures of costs and benefits, a novel model-driven approach of calibrated behavioral tasks and neuroimaging is needed to characterize the specific influence and representation of effort costs in these decisions.

2.3 A *Prospective Effort* Paradigm for Testing Effort-Based Valuation

As reviewed in the previous section, effort-based decision making research has proposed that energetic requirements generally reduce value signals in cortex and reduce behavioral response rates. However, to date, there has been no systematic separation of effort costs from other types of cost in mixed outcome decisions. To address this confound, we designed an effort-based valuation task that asked subjects to make prospective decisions about physical efforts. Critically, we trained subjects on a parametric physical effort task prior to effort-based valuation. This prospective paradigm presents decision-makers a trade-off between potential work and reward, an attempt to bring effort-based valuation tasks closer to ethologically relevant decision-making scenarios.

2.4 Pilot Experiments: Materials and Methods

2.4.1 Pilot Experiments: Participants

Three samples of healthy, right-handed subjects recruited from the University of Texas at Austin community participated in the experiment. The first pilot sample included 12 subjects (mean age = 19.6 years, standard deviation = 3.4 years, 7 females). The second sample included 23 subjects (mean age = 21.6 years, standard deviation = 1.32 years, 12 females). The third sample included 15 subjects (mean age = 20.1 years, standard deviation = 2.51 years, 7 females). Informed consent was collected prior to the experiment. All participants had normal or corrected-to-normal vision, and reported no history of psychiatric diagnoses, and neuralgic or metabolic illnesses. The Human Subjects and Institutional Review Board at the University of Texas at Austin approved all procedures.

2.5 Pilot Experiments: Behavioral Paradigm

The introduction and baseline force measurement protocol was identical for all three experiments described in this chapter.

Stimuli and Introduction: Prior to the experiment, subjects provided informed consent and were endowed with $10 cash. Subjects were instructed that they were participating in a study about risk preferences in economic choices. Stimulus presentation and response collection were implemented with custom MATLAB code and the Psychophysics toolbox (Brainard, 1997)

Baseline Force Measurement: First, subjects were prompted to squeeze the dynamometer with their right hand as hard as possible in three intervals of two seconds interspersed with periods of rest for two seconds. The calibration procedure was performed without feedback or incentive. The average force assessed by this procedure was considered the subject's maximum voluntary contraction (MVC) force for calibration of the training and test task phases. After calibration, subjects were shown a display with real-time force feedback for demonstration purposes.

2.5.1 Pilot Experiments: Physical Effort Training

All training phases were designed to familiarize subjects with the difficulty of performing a range of effort levels. Subjects learned to associate color and height cues with effort levels they performed, critical for subsequent prospective effort choices. We altered the levels of effort in the physical effort training phase across samples to achieve a range of success rates. A consistent range of average parametric effort success was desired to test the effect of prospective effort upon risk taking and delay discounting in future experiments described in Chapters 3 and 4.

Experiment 1 Based on previous effort-based valuation studies that employed a physical grip paradigm, our first experiment tested subjects with four levels of difficulty (30, 50, 70 and 90% of calibrated MVC, 80 randomized trials, 20 trials of each difficulty level.) To successfully complete a trial, subjects were required to exert force at or above the given effort level for at least 1 second within a 2 second response period. Subjects received real-time effort feedback during production and success or failure to meet effort goal feedback on a trial-by-trial basis.

Experiments 2 and 3 Based the results of experiment 1, we adjusted our range of effort difficulty. Subjects were tested with five levels of effort difficulty (30, 40, 50, 60 and 70% of calibrated MVC, 80 randomized trials, 20 trials of each difficulty level.) Again, to successfully complete a trial, subjects were required to exert force at or above the given effort level for at least 1 second within a 2 second response period. Subjects received real-time effort feedback during production and success or failure to meet effort goal feedback on a trial-by-trial basis.

2.5.2 Pilot Experiments: Prospective Effort Mixed Gambles

We adapted a mixed gambles paradigm to test the effects of prospective effort attributes in a risky valuation task. In our first sample, we presented mixed gambles at four levels effort and one level of fixed probability. Experiments 2 and 3 presented five levels of prospective effort alone.

Experiment 1 During this phase, subjects were instructed to rate the subjective attractiveness of prospective effort mixed gambles. Each mixed gamble presented three components: a potential gain in addition to their endowment ($2-$10 in six linearly spaced increments), and a potential loss from their endowment ($1-$5 in six linearly spaced increments), contingent upon performing one of five levels of effort as performed in the training session (30, 50, 70, and 90% of calibrated MVC) successfully five times in a row. See figure 3.2 for an overview of the task. All 36 combinations of potential gain and loss were presented at each of the four effort levels, 144 prospective effort mixed-gamble trials in total. Additionally, we interspersed prospective effort trials with trials from an identical 36 trial choice set that reflected no effort prospect. Subjects were instructed that these trials offered an equal probability of gain or loss that would be resolved with a coin flip. Trial order and inter-stimulus interval timing was determined from an efficiency calculation for the prospective effort contrast that split 180 trials into five runs of 36 trials each. Potential gain and loss were subsequently randomized across all trials. To encourage participants to reflect on the subjective attractiveness of each mixed prospect rather than revert to a fixed decision rule (e.g., accept prospect only if potential gain twice as large as potential loss), we asked subjects to indicate one of four responses to each gamble (strongly accept, weakly accept, weakly reject, and strongly reject) as quickly as possible with a standard keyboard. Subjects were instructed that one trial would be selected at random at the end of the experiment and resolved according to their choice.

Experiment 2 and 3 During this phase, subjects were instructed to rate the subjective attractiveness of prospective effort mixed gambles. Each mixed-gamble presented three components: a potential gain in addition to their endowment ($2-$10 in six linearly spaced increments), and a potential loss from their endowment ($1-$5 in six linearly spaced increments), contingent upon performing one of five levels of effort as performed in the training session (30, 40, 50, 60 and 70% of calibrated MVC) successfully five times in a row. All 36 combinations of potential gain and loss were presented at each of the five effort levels, 180 prospective effort mixed-gamble trials in total. Trial order was randomized to split 180 trials into five runs of 36 trials each. To encourage participants to reflect on the subjective attractiveness of each mixed prospect rather than revert to a fixed decision rule (e.g., accept prospect only if potential gain twice as large as potential loss), we asked subjects to indicate one of four responses to each gamble (strongly accept, weakly accept, weakly reject, and strongly reject) as quickly as possible with a standard keyboard.

Subjects were instructed that one trial would be selected at random at the end of the experiment and resolved according to their choice.

2.6 Pilot Experiments: Behavioral Results

2.6.1 Effort Training Success

Increased effort requirements reduced subjects' average performance on individual trials during the effort grip force training phase, as depicted in figure 2.1. In our initial pilot sample, the highest effort prospect was too difficult for many subjects to complete as required. Accordingly, we adjusted the range of prospective value levels for our subsequent samples. In samples 2 and 3, we found a desired linear relationship between average success during training and effort level.

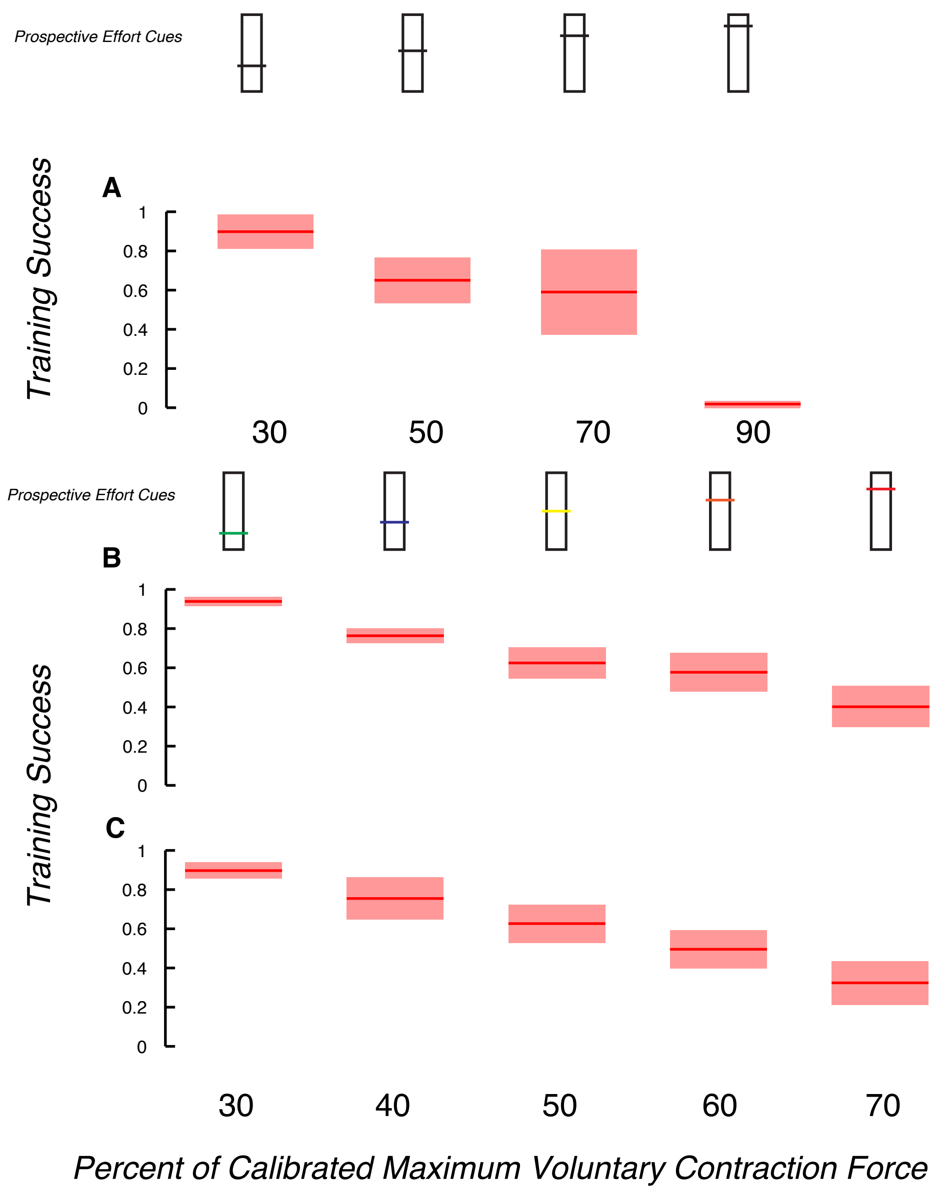

Figure 2.1: *Subjects' average effort grip force performance reflect modulation by effort level. Top, depcitions of effort cues tested during the training phase. (A) Average training success in our initial pilot sample (n=12). (B) Average training success in our second pilot sample (n=23). (C) Average training success in our final pilot sample (n=13). Shaded color bars around group averages indicate standard error of the mean.*

2.6.2 Prospective Effort Mixed Gambles

Subjects overall willingness to take gambles reflected an effect of prospective risk cost, whereby greater prospective effort reduced gamble acceptance. Figure 2.2 illustrates overall behavior during the prospective effort mixed gambles phase in our pilot samples. Overall, subjects willingness to accept gambles reflected sensitivity to the ratio of gains and losses. However, subjects were insensitive to expected value at extreme effort levels of prospective effort, such as those examined in sample 1. In sample 1, subjects' average gamble acceptance at equal probability of win or loss (coin flip) was similar to other studies of valuation under risk (Tom et al., 2007; De Martino et al., 2010; Canessa et al., 2013).

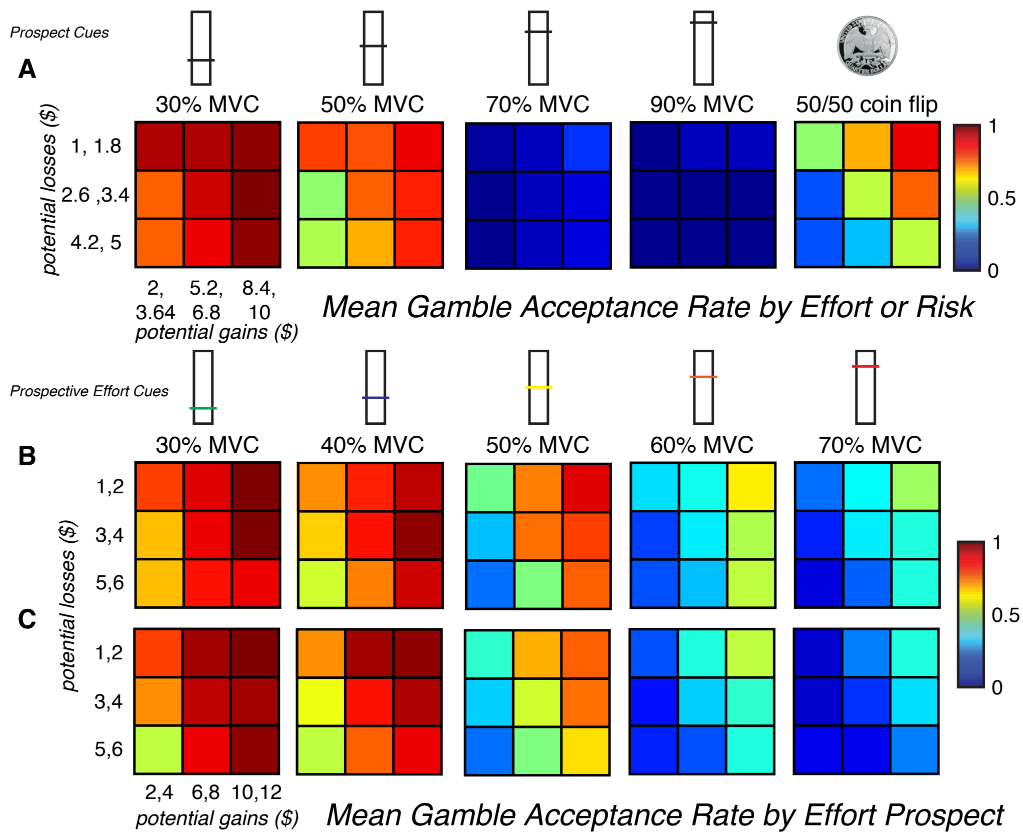

Figure 2.2: *Heatmaps depict average gamble preferences and median average reaction times across levels of prospective effort or risk for all subjects. Each level is represented with potential gains and losses collapsed across levels of gain and loss magnitude. (A) Gamble behavior from our intital pilot sample reflected reduced success with extreme prospective effort levels and consistent risk preferences in the coin flip condition with previous studies. (B-C) Gamble behavior in subsequent samples found a consistent relationship between willingness to face an effort challenge to resolve a gamble. Additionally, on average, subjects were sensitive to the expected value of a gamble within an effort level.*

2.7 Discussion

We adapted a mixed gambles decision task from behavioral economics to assess the influence of prospective effort upon choice. In multiple pilot studies, we found reduced willingness to take risk under prospective effort challenges. We developed this task to address a critical shortcoming in the effort-based decision making literature, failure to separate choices about effort from immediate effort production or anticipation of outcome. Our behavioral results suggest that gamble behavior under carefully adjusted prospective effort reflects the imposition of a graded effort cost. In summary, the prospective effort paradigm provides a novel approach to extend the literature of effort-based valuation. In the following chapters, I describe two set of experiments that directly test the effect of prospective effort costs upon well known aspects of valuation, decision making under risk and delay.

Chapter 3

Prospective Effort and Decision Making Under Risk

3.1 Chapter Summary

This chapter describes an experiment designed to test the behavioral and neural correlates of effort-based valuation with the prospective effort paradigm described in the previous chapter. In this experiment, subjects reflected upon the value of monetary gamble prospects resolved by prospective effort or risk challenges. Effort and risk were hypothesized to weigh upon subjects valuation as a graded cost, reflected in choice behavior and neural activity. Model-based analyses revealed behavioral and neural correlates of value discounting associated with effort and risk and provide new evidence for the general understanding of neural substrates of economic valuation processes. The following text presents an adapted manuscript related to this experiment currently in preparation for peer-review.

3.2 Abstract

Adaptive choice behavior in a dynamic world requires simultaneous consideration of the energy expenditure of an action with other potential costs

and benefits. Compared to risk and delay, the neural substrates of effort-based valuation in economic decisions remain poorly understood. Previous human neuroimaging studies suggest that effort-based decisions involve the ventral striatum and anterior cingulate cortex (ACC), structures previously implicated in motivated behavior by animal studies. However, neuroimaging tasks employed to localize effort valuation have typically confounded effort costs with the delay to outcome or anticipation of subsequent effort production. To resolve whether effort-based decisions specifically recruit these regions, we designed a novel prospective effort choice task. Subjects underwent functional neuroimaging while they decided to accept or reject gambles that offered the opportunity to win or lose money. Gamble outcome was contingent upon performance of one of five previously trained physical effort levels at the end of the session. Increasing effort prospects associated with gambles reduced subjects willingness to gamble and increased their sensitivity to potential losses over potential gains. Prospective efforts costs were represented in the anterior insular cortex, dorsal premotor cortex and motor planning areas. Prospective effort representation overlapped with representation of potential gains in ventromedial prefrontal cortex (vmPFC) and gains and losses in medial frontal cortex and motor planning areas. Contrary to previous reports in the human literature that focus upon ACC as the locus of effort-based valuation, our results support a role for dorsal premotor structures in effort-based inferences, whereby motor representations and abstract value signals interact during choice.

3.3 Introduction

Foraging, a fundamental animal behavior, requires balancing efforts to obtain rewards(Rigoux and Guigon, 2012). When presented with choices among actions, optimal behavior requires a valuation process that links actions and potential outcomes to guide choice. Accordingly, animals are sensitive not merely to expected rewards in choice tasks, but also effort requirements, such as scaling a barrier or repeating an action (Salamone, 2009; Walton et al., 2006) to obtain them. Effort describes the cost in energetic resources associated with an action. It may involve cognitive or physical labor, each assumed to reflect a limited capacity at the time of choice. Here, we focus upon the role of physical effort in choice. Compared to other common costs like risk and temporal delay, its influence upon the neural and behavioral correlates of valuation processes remains poorly understood.

Leading theories of foraging behavior and economic decision making propose that animals seek to minimize costs to maximize utility. To accomplish this, theoretical accounts and experimental evidence emphasize the formation of abstract value signals from a cost-benefit analysis to guide choice among alternatives. Neuroimaging and animal studies of valuation often identify value-related signals within a core network of basal ganglia and frontal cortical regions. However, lesion studies in animals suggest that effort-based valuation recruits distinct structures (Walton et al., 2007). For example, when effort and delay costs are modulated independently, animals with lesions to either ACC or orbital frontal cortex (OFC) exhibit selective impairment of valuation processes (Rudebeck et al., 2006). Additional evidence from rat and human studies has linked activity within striatum to effortful behavior (Salamone et al., 2007; Croxson et al., 2009; Kurniawan et al., 2010; Schouppe et al., 2014).

Together, these results support at least a partial dissociation of effort-based valuation from other costs. However, effort-based tasks in human and animal populations have typically confounded effort costs with delay and anticipation of subsequent effort production. For example, notable effort-based studies varied the number of actions required to obtain reward (Croxson et al., 2009; Kennerley and Wallis, 2009). Even when effort cost is manipulated independently, neuroimaging studies have inconsistently ascribed effort-based cost-benefit valuation to striatum (Croxson et al., 2009) ACC (Prevost et al., 2010), insular cortex (Meyniel et al., 2013), and OFC (Burke et al., 2013). Furthermore, these studies have not offered effort-based choices separated from the resolution of an immediate outcome, nor addressed the potential confound of decision difficulty and time spent on task. To address these issues, we designed an fMRI experiment with a prospective effort paradigm that separated effort-based valuation from effort execution, anticipation and reward receipt.

3.4 Materials and Methods

3.4.1 Participants

Forty-six healthy, right-handed subjects recruited from the University of Texas at Austin community participated in the experiment. Six subjects were excluded from further analyses due to excessive head movement (2), MRI artifacts (2) or failure to meet behavioral criteria described below (2). The remaining forty subjects comprised the sample group for our fMRI analyses (mean age = 22.4 years, standard deviation = 2.94 years, 20 females). Sample size was determined a priori by a power analysis for a contrast of interest (parametric prospective effort) from a pilot study of 13 subjects (mean age = 21.3 years, standard deviation 2.31 years, 7 females) with the fMRIpower software package (Mumford and Poldrack, 2014). Each subject provided informed consent prior to the experiment. All participants had normal or corrected-to-normal vision, reported no history of psychiatric diagnoses, and neuralgic or metabolic illnesses. The Human Subjects and Institutional Review Board at the University of Texas at Austin approved all experimental procedures.

3.4.2 Behavioral Paradigm

Stimuli and Introduction: Prior to the experiment, subjects were endowed with $20 cash. Subjects were instructed that they were participating in a study about preferences in economic choices. Stimuli presentation and subject response collection were implemented with custom MATLAB code and the Psychophysics toolbox (Brainard, 1997)

Baseline Force Measurement: Once inside the MRI scanner, each subjects maximum voluntary contraction (MVC) force was assessed with an MR-compatible dynamometer (BIOPAC TSD121B-MRI, BIOPAC Systems Inc., USA). Subjects were prompted to squeeze the dynamometer with their right hand as hard as possible in three intervals of two seconds interspersed with periods of rest for two seconds. The calibration procedure was performed without feedback or incentive. The average force assessed by this procedure was considered the subjects MVC for calibration of the training and test task phases. After calibration, subjects were shown a display with real-time force feedback for demonstration purposes.

Effort Training: The effort training phase is summarized in figure 3.1. This phase was designed to familiarize subjects with the difficulty of performing a range of effort levels. Subjects learned to associate color and height cues with effort levels they performed, critical for subsequent prospective effort choices. Briefly, during the training run, subjects completed effort production trials without incentive at five levels of difficulty (30, 40, 50, 60 and 70% of calibrated MVC, 80 trials from one of 5 orders optimized for event-related fMRI, 16 trials of each difficulty level.) To successfully complete a trial, subjects were required to exert force at or above the given effort level for at least 1 second of total time within a 2 second response period. Subjects received real-time feedback of effort provided during production and success or failure to meet the effort goal on a trial-by-trial basis.

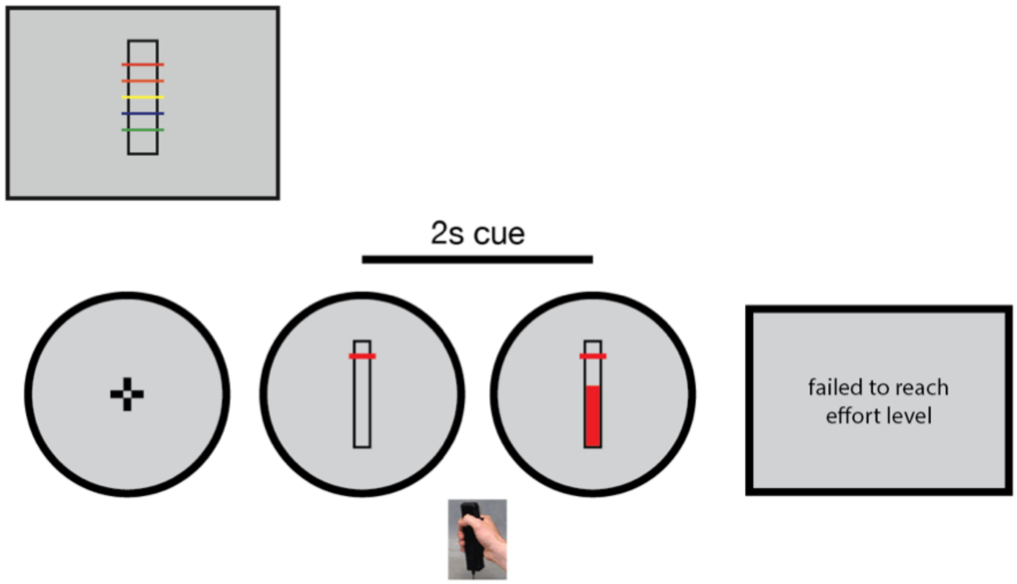

Figure 3.1: Subjects were presented with one of 5 unique color and height lines across a familiar grip force display (top left). When the stimulus was present, subjects attempted to provide enough grip force to raise a red bar that reflected the amount of force applied in real-time above the line. Subjects were required to maintain a force level at or above the line for at least one second of total time within a two second interval to successfully complete a trial. Success or failure feedback was provided after each trial.

Prospective Effort Mixed Gambles: During this phase, subjects were instructed to rate the subjective attractiveness of prospective effort mixed gambles. Each mixed gamble presented three components: a potential gain in addition to their endowment (\$2-\$12 in \$2 increments), and a potential loss from their endowment (\$1-\$6 in \$1 increments), contingent upon performing one of five levels of effort as performed in the training session (30, 40, 50, 60 and 70% of calibrated MVC) successfully five times in a row. See figure

3.2 for an overview of the task. All 36 combinations of potential gain and loss were presented at each of the five effort levels, 180 prospective effort mixed gamble trials in total. Trial order and inter-stimulus interval timing was determined from an efficiency calculation for the prospective effort contrast that split 180 trials into 5 runs of 36 trials each (Kao et al., 2009). Potential gain and loss were subsequently randomized across all trials. To encourage participants to reflect on the subjective attractiveness of each mixed prospect rather than revert to a fixed decision rule (e.g., accept prospect only if potential gain twice as large as potential loss), we asked subjects to indicate one of four responses to each gamble (strongly accept, weakly accept, weakly reject, and strongly reject) as quickly as possible with a four-button response box. Subjects were instructed that one trial would be selected at random at the end of the experiment and resolved according to their choice.

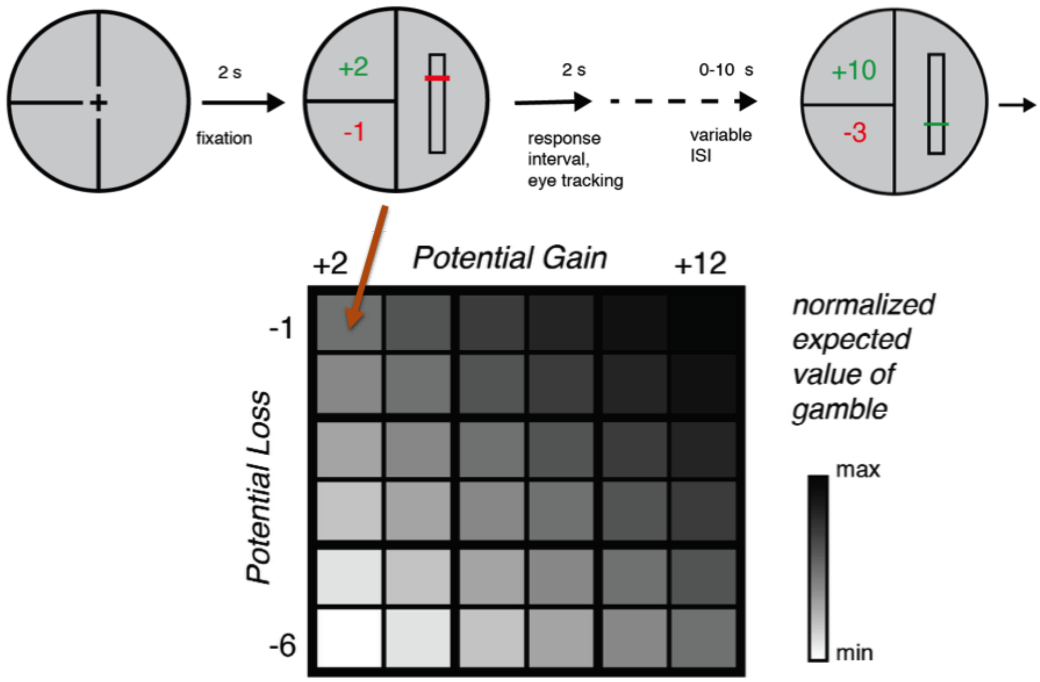

Figure 3.2: Subjects accepted or rejected the prospect of facing a monetary gain or loss contingent upon successful performance of one of the 5 previously trained effort levels. Combinations of potential gain and loss were drawn at random for each effort level from an asymmetric choice set shown below.

Prospective Risk Mixed Gambles: During this phase, subjects were instructed to rate the subjective attractiveness of prospective risk mixed gambles. Critically, by design this phase always followed the effort mixed gambles phase. This order was intended to prevent subjects from reflecting upon effort mixed gambles as effort-based prospects, rather than gambles with fixed win probabilities. Each mixed-gamble presented three components: a potential gain in addition to their endowment (\$2-\$12 in \$2 increments), and a potential loss from their endowment (\$1-\$6 in \$1 increments), contingent upon one of five levels of win probability (10, 30, 50, 70 and 90% probability of winning). See figure 3.3 for an overview of the task. As in the effort mixed gambles task, all 36 combinations of potential gain and loss were presented at each of the five risk levels, 180 prospective risk mixed-gamble trials in total. Trial order and inter-stimulus interval timing was determined from an efficiency calculation for the prospective effort contrast that split 180 trials into five runs of 36 trials each (Kao et al., 2009). Potential gain and loss were subsequently randomized across all trials. To encourage participants to reflect on the subjective attractiveness of each mixed prospect rather than revert to a fixed decision rule (e.g., accept prospect only if potential gain twice as large as potential loss), we asked subjects to indicate one of four responses to each gamble (strongly accept, weakly accept, weakly reject, and strongly reject) as quickly as possible with a four-button response box. Subjects were instructed that one trial would be selected at random at the end of the experiment and resolved according to their choice.

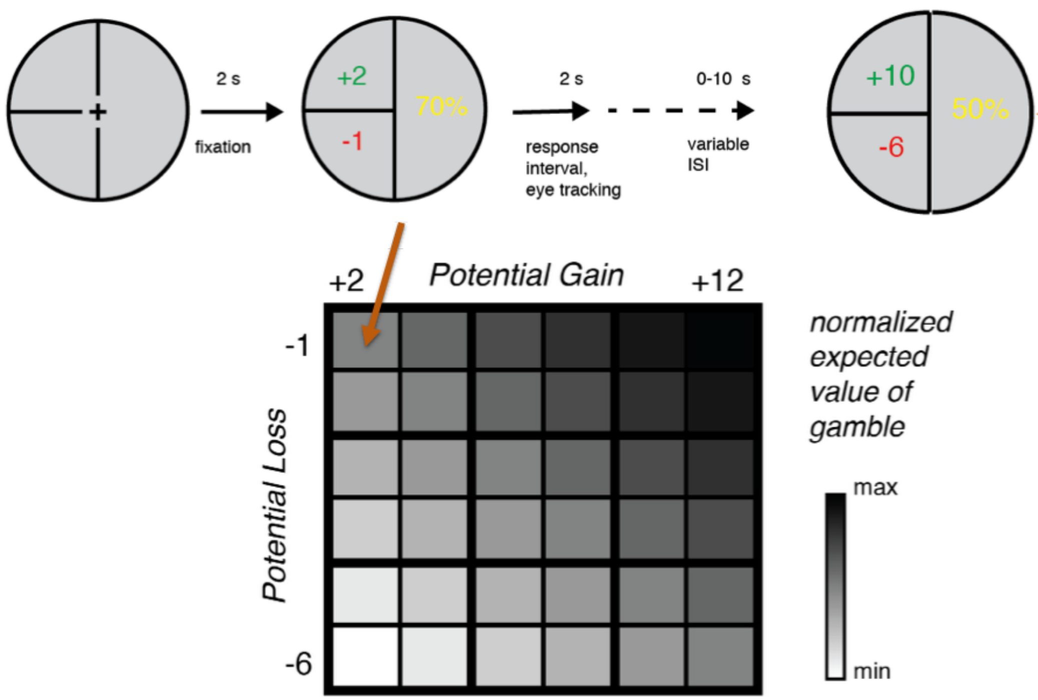

Figure 3.3: Subjects accepted or rejected the prospect of facing a monetary gain or loss contingent upon the resolution of one of five probabilities of winning. Combinations of potential gain and loss were drawn at random for each effort level from an asymmetric choice set shown below.

Confidence Ratings: After the mixed gambles phases and while still in the scanner, subjects were asked to rate how confident they were that they could perform each of nine levels of effort (spanning 10-90% of their MVC in 10% increments) five times in a row, as required to resolve gambles successfully from the prospective effort mixed gamble phase.

Mixed Gamble Resolutions: At the end of the task, one trial was selected at random from all effort mixed gambles. If the subject had accepted the selected gamble, they were required to attempt to successfully perform the associated effort level five times in a row as practiced during the training phase. If successful, a subject earned the amount of potential gain associated with the trial. If they were not successful, the subject lost the amount of money associated with potential loss from their initial endowment. As instructed at the start of the experiment, if the subject had rejected the randomly selected gamble, they were allowed to keep their initial endowment and the experiment ended without additional effort production trials.

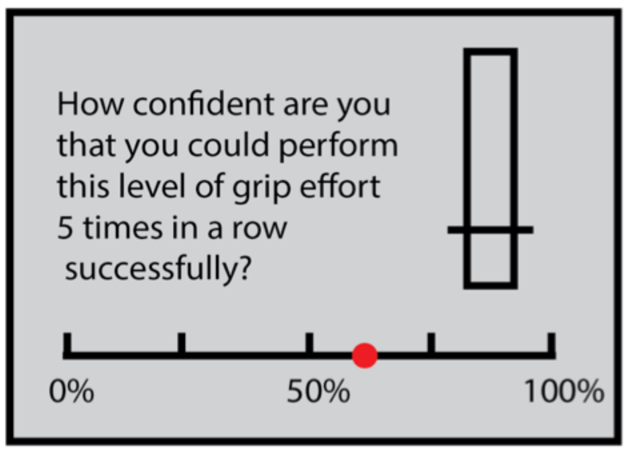

Figure 3.4: Subjects rated their confidence in performing a range of effort levels as required in the prospective effort mixed gambles task.

3.4.3 Behavioral Analyses

Behavioral analyses focused upon preferences during prospective risk and effort gamble evaluation. We tested subjects overall willingness to gamble (proportion of gambles accepted) prior to other behavioral analyses. This test revealed two subjects that failed to meet a predetermined behavioral threshold (accepted or rejected more than 95% of all gamble trials) and excluded them from further analyses. From the training phase, we calculated mean response accuracy (percentage of successful effort trials). From the prospective effort gamble phase, we calculated acceptance rate by prospective effort, gain and loss level, and reaction time in milliseconds. Statistical analyses (linear regression analyses, ANOVAs and t tests) were performed with custom analyses within MATLAB (The Mathworks, Natick, MA).

3.4.4 Image Acquisition

Imaging data were acquired on a 3 Telsa Skyra MRI scanner system (Siemens) with a 32-channel head coil. Anatomical images for registration to Montreal Neurological Institute template space were acquired with a high-resolution magnetization prepared rapid gradient echo (MPRAGE) pulse sequence (TR = 1900 ms, TI = 900 ms, TE = 2.43 ms, flip angle = 9°, FOV = 256, voxel size 1.0 x 1.0 x 1.0 mm). Functional images were acquired collected using a T2* weighted multiband (Moeller et al., 2010) echo-planar imaging sequence (TR= 1000 ms, multiband acceleration factor= 4, iPAT parallel acceleration factor = 2, TE=30 ms, flip angle = 63°, FOV=230, voxel size 2.4 x 2.4 x 2.4 mm). During functional scans, fifty-six gapless axial slices were positioned 30°off the anterior commissure-posterior commissure line to reduce frontal signal dropout (Deichmann et al., 2003). Higher-order shimming was used to reduce susceptibility artifacts.

3.4.5 fMRI Data Preprocessing

Data preprocessing was performed in a custom analysis stream that included components of the FreeSurfer and FSL neuroimaging analysis packages. First, raw imaging data in DICOM format were converted to NIFTI format. Functional images were aligned with the FSL MCFLIRT tool to obtain six motion parameters that correspond to the x-y-z translation and rotation of the brain over time. Skull was removed from functional images with the FSL brain extraction tool (*BET*) and from T1-weighted MPRAGE images with FreeSurfer (*autorecon1*). Spatial smoothing of functional images was performed with a Gaussian kernel with a full-width half maximum of 5 mm. Data and design matrices were high-pass filtered with a Gaussian-weighted least-squares straight line fit with a cutoff period of 100 s. Grand-mean intensity normalization of each functional image volumes entire four-dimensional data set was performed by a single multiplicative factor. Each subjects functional image volumes were registered to their T1-weighted MPRAGE volume with a boundary-based registration method implemented in FSL5 (*BBR*). Each subjects resulting T1-weighted image was then registered to the MNI152 2mm template according to a linear registration algorithm implemented in FSL with 12 degrees of freedom (*FLIRT*). These two registration steps were concatenated to obtain a functional-to-standard space registration matrix for each functional image volume.

3.4.6 fMRI Data Analyses

Whole-Brain Analyses We focused on the choice period to examine neural activity related to prospective effort and valuation. We used general linear models to assess the relationship of BOLD data to experimental variables, model predictions and subjects choices. A whole-brain parametric model (GLM1) modeled 3 orthogonal parametric regressors: prospective gain, prospective loss, prospective effort level, to identify brain regions whose activation or deactivation correlated with the size of each variable. Reaction time was modeled with two additional regressors: demeaned within-run average reaction time and demeaned trial-by-trial reaction time minus within-run mean reaction time (Mumford and Poldrack, 2014). Additional regressors of no interest modeled trials without behavioral responses and unconvolved motion parameters (x-y-z translation and rotation of the brain over time).

To further illustrate the interaction of prospective effort within regions present in whole-brain parametric analysis (GLM1), we performed a second whole-brain analysis (GLM2) that collapsed all trials by prospective effort levels. Each subjects gamble trials were collapsed into a 3×3 matrix, whereby each cell contained all trials from all levels of gain and loss. GLM2 modelled trials from each matrix cell with a parametric effort prospect regressor and additional regressors for reaction time and motion parameters as in GLM1. A third whole-brain GLM analysis (GLM3) also collapsed all trials into a 3×3 matrix of gain and loss levels to test for mean activation related to each of 9 combinations of gain and loss that reflect a range of expected value outcomes. Similarly, we included additional regressors for reaction time and motion parameters as in GLM1.

Finally, a fourth and fifth set of whole-brain analyses (GLM4, GLM5) modeled a parametric regressor for subjective value predicted by discount model for the effort mixed gambles and risk mixed gambles phases. We calculated a subjective value for each trial according to a generalized hyperbolic discount function (Talmi and Pine, 2012):

$$SV = \frac{Gain}{1 + (Effort \times Loss)}$$

whereby subjective value (SV) reflects the size of potential gain, discounted by effort and potential loss. Subjective value for risk mixed gambles followed a separate discounting equation previously implicated in probability discounting (Talmi and Pine, 2012):

$$SV = (Gain - Loss) \times p(win)$$

whereby subjective value (SV) reflected the difference in potential gain and loss multiplied by probability of winning for each gamble. Again, in each subjective value model, we included additional regressors for reaction time and motion parameters as in GLM1.

Region of Interest Analyses (GLM1): We tested for regionally specific activations related to parametric regressors from GLM1 within several brain areas reported in previous studies of effort-based valuation and valuation under risk. These analyses are summarized below and in table 3.5.We tested several a priori ROIs for anticipation of gains, losses or effort based on peak activations in previous tasks with similar designs. We first tested an *a priori* ROI from the conjunction between increasing activity for increasing gains and decreasing activity for decreasing losses from (Tom et al., 2007) around peak MNI coordinates in mPFC (x = -6; y = 38; z = -10). Three additional a priori ROIs were tested from (Canessa et al., 2013), anticipation of gains in bilateral caudate nucleus (L, x = -14; y = 14; z = 10), (R, x = 18; y = 18; z = 2) and anticipation of losses in bilateral insula lobe (L, x = -36; y = -14; z = 10), (R, x = 36; y = -28; z = 18) and right amygdala (x = 28; y = 2; z = -10). We also examined activity within *a priori* ROIs for anticipation of effort based on previous effort-based valuation studies. These ROIs included two ACC ROIs related to effort-discounted reward from (Croxson et al., 2009) (x = -12; y = 28; z = 14) and (Prevost et al., 2010) (x = 6; y = 24; z = 28), two SMA ROIs related to anticipation of greater effort (x = -6; y = -7; z = 64) (Kurniawan et al., 2013), (x = -9; y = 8; z = 52) (Burke et al., 2013), and a frontal pole ROI related to evaluation of compound risk and effort trials (x = -9; y = 62; z = 22) (Burke et al., 2013). All a priori ROIs were defined as one or two (bilateral) 8 mm spheres centered at the peak MNI coordinates above.

Multivariate Pattern Analysis: A separate set of analyses applied machine-learning algorithms to attempt to decode levels of prospective effort during training and at choice in the prospective effort mixed gambles task. Due to artifacts in the training data, one subject was disqualified from further analysis. Beta estimates from the remaining 39 subjects were obtained for each trial at the five levels of prospective effort. Whole-brain linear support vector regression analyses within subject and across subjects were conducted with the *scikit-learn* package in Python. Initial analyses were performed within-subject on training data, with subjects' data split into two halves for regression machine training and testing. For the cross-subject analyses, we sequentially trained the regression machine with all runs of the prospective effort mixed gambles task from 38 subjects. Finally, the regression machine was then tested on labeling the remaining left out subject's data.

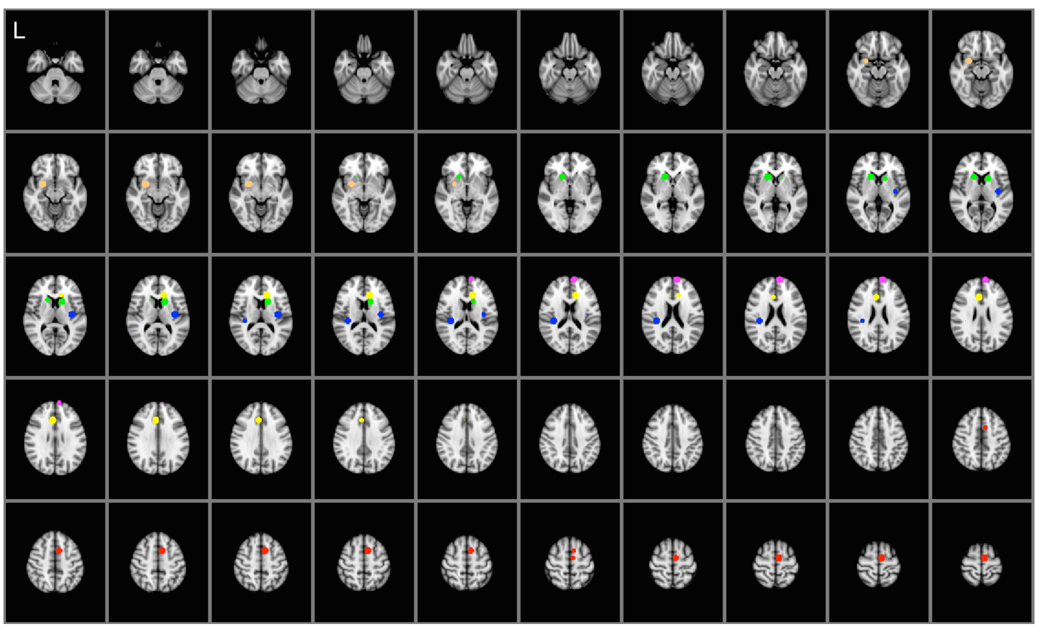

Figure 3.5: Locations of spherical region of interest analyses based on previous effort-based valuation studies overlaid on axial sections of the MNI-152 template atlas. Spheres are colored according to the anatomical label in each study. Green = striatum, caudate nucleus, pink = frontal polar cortex, red = SMA, yellow = ACC, blue = insula lobe, and orange = right amygdala

We also examined activations within three extensive anatomical ROIs previously related to effort or valuation processes. These ROIs were defined from unthresholded Harvard-Oxford atlas masks within FSL. These Harvard-Oxford atlas masks included (1) a pre-hypothesized medial frontal cortex (mPFC), and exploratory (2) combined insular cortex and frontal operculum cortex, (3) exploratory combined paracingulate cortex, superior frontal gyrus, juxtapositional lobule cortex (SMA) and cingulate gyrus (anterior division), and (4) exploratory combined precentral gyrus and postcentral gyrus.

Region of Interest Analyses (GLM2, GLM3): To illustrate activity related to anticipation of effort at fixed levels of potential gains and losses, we performed GLM analyses within functionally defined ROIs derived from the results of GLM1. Functional ROIs were defined with the conjunction-null test (Nichols et al., 2005) between individual statistical maps ($p > 0.05$, whole-brain, cluster corrected) of activation for effort and activation for gains and deactivation for losses, or activation for losses and deactivation for gains (refer to table 3.4). These analyses were used to illustrate the direction of activation within these ROIs related to variance of outcomes and mean activation or prospective effort, not for the purpose of statistical inference (Kriegeskorte et al., 2009).

3.5 Behavioral Results

3.5.1 Behavior: Effort Training

Increased effort requirements reduced subjects' average performance on individual trials during the effort grip force training phase, as depicted in figure 3.1, (F(4,195) = 13.71, p <0.001). Subjects' training behavior was well described by a linear model whereby increased effort level predicted reduced training success: ($\beta = -3.1, t(198) = -7.3, p < 0.001$), effort level explained a significant portion of variance in training performance ($R^2 = 0.21F = 53.1, p < 0.001$). In post-task ratings of effort performance confidence prior to effort mixed gamble resolution, increased effort requirements also reduced subjects' average confidence, (F(8,351) = 20.1, p </ 0.001), as depicted in figure 3.4. Similarly, we found that subjects' post-task confidence ratings were well described by a linear model whereby effort level predicted confidence: ($\beta = -5.32, t(358) = -12.33, p < 0.001$), effort level explained a significant portion of variance in confidence ratings ($R^2 = 0.30F = 152, p < 0.001$). Figure 3.6 illustrates average training performance and post-task confidence behavior across subjects.

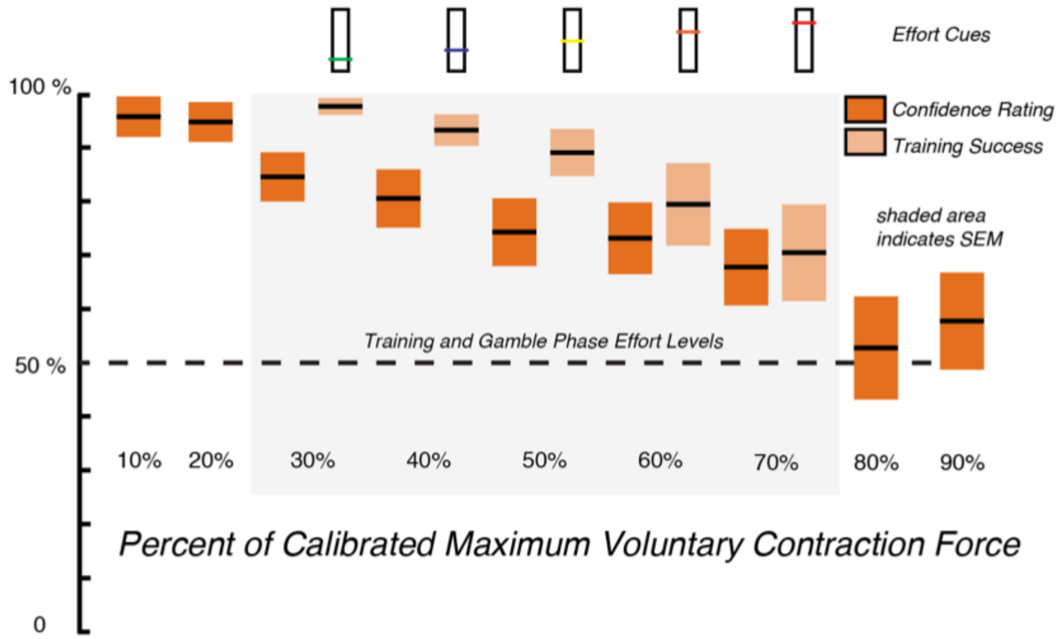

Figure 3.6: *Subjects' average effort grip force performance (light orange) and post-task confidence ratings (dark orange) reflect modulation by effort level. The effort cues tested during the training phase are depicted at top. Performance and ratings for tested levels are shaded in gray. Shaded color bars around group averages indicate standard error of the mean.*

3.5.2 Behavior: Prospective Effort mixed gambles

Subjects overall willingness to take gambles reflected an effect of prospective effort cost over all levels of potential gain and loss ($F(4{,}195) = 29.67$, $p < 0.001$), whereby greater prospective effort reduced gamble acceptance. Figure 3.7 illustrates overall behavior during the prospective effort mixed gambles phase. As expected, subjects' willingness to accept the chance of performing an effort to resolve a gamble reflect the level of prospective effort. Additionally, subjects willingness to accept gambles reflected sensitivity to the ratio of gains and losses. Subjects' reaction times scaled with the size of the expected value and level of prospective effort. Generally, the longest median average reaction times were associated with prospective effort mixed gambles that subjects were on average closer to indifference (50% acceptance rate).

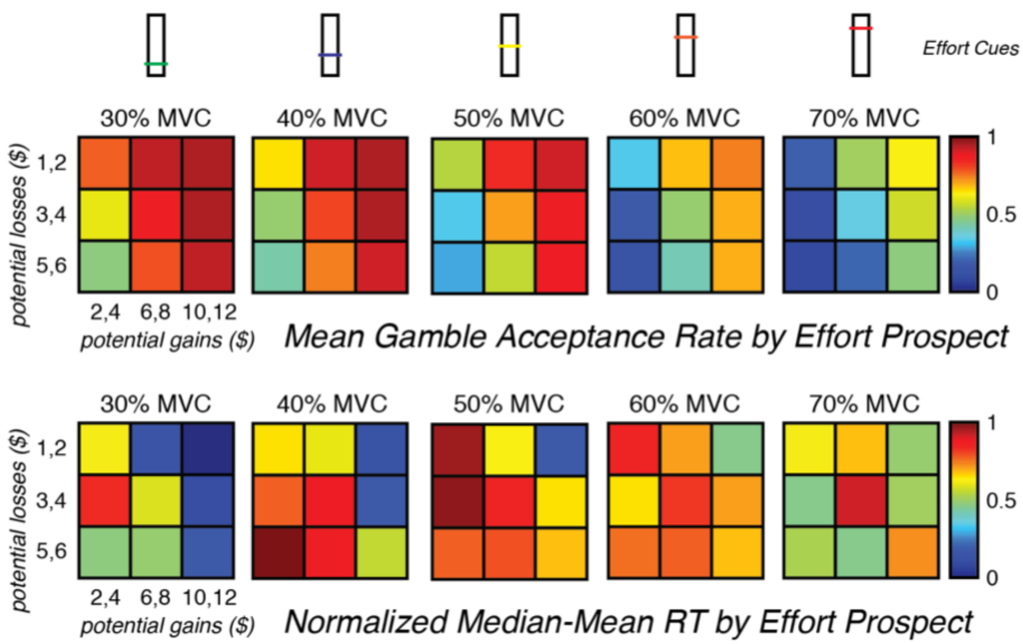

Figure 3.7: *Heatmaps depict average gamble preferences and median average reaction times across levels of prospective effort for all subjects. Each level is represented with potential gains and losses collapsed across magnitude. Generally, increasing effort prospects reduce willingness to accept prospective effort gambles.*

3.5.3 Behavior: Prospective Risk mixed gambles

As expected, subjects overall willingness to take gambles reflected an effect of prospective risk cost over all levels of potential gain and loss (F(4,195) = 24.41, p <0.001), whereby greater prospective effort reduced gamble acceptance. Figure 3.8 illustrates overall behavior during the prospective risk mixed gambles phase. As in the previous prospective effort mixed gambles phase, subjects willingness to accept gambles reflected sensitivity to the ratio of gains and losses. However, subjects were more sensitive to the range of prospective risk levels than prospective effort levels, illustrated by greatly reduced or increased average acceptance rates at extreme risk levels. Subjects' average gamble acceptance at equal probability of win or loss was similar to other studies of valuation under risk (Tom et al., 2007; Canessa et al., 2013; De Martino et al., 2010) Subjects' reaction times scaled with the size of the expected value and level of prospective effort. Across subjects, the longest normalized reaction times were associated with prospective effort mixed gambles that subjects were on average closer to indifference (50% acceptance rate), as illustrated in figure 3.9.

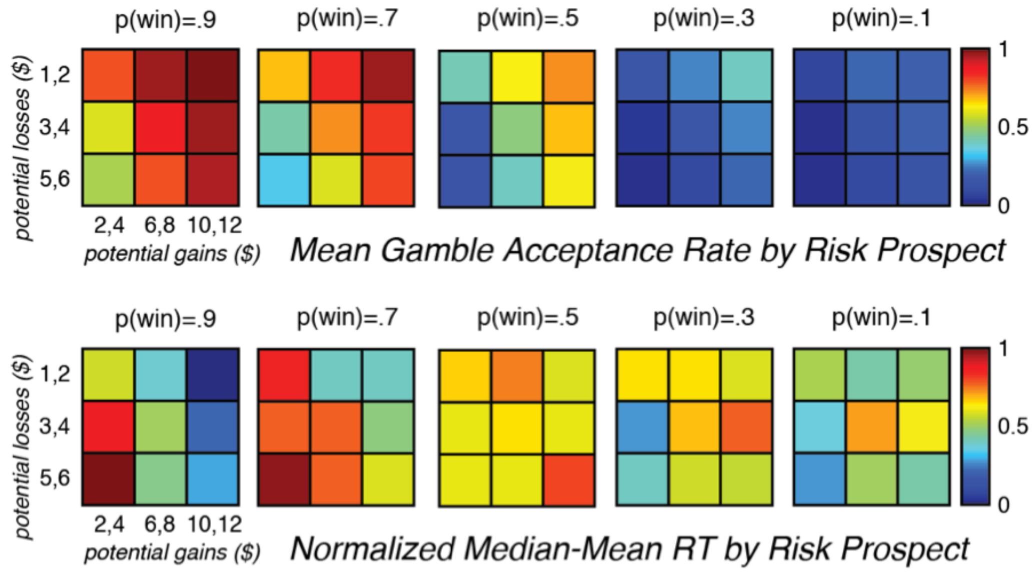

Figure 3.8: *Heatmaps depict average gamble preferences and median average reaction times across levels of prospective risk for all subjects. Each level is represented with potential gains and losses collapsed across magnitude. Generally, increasing effort prospects reduce willingness to accept prospective risk gambles.*

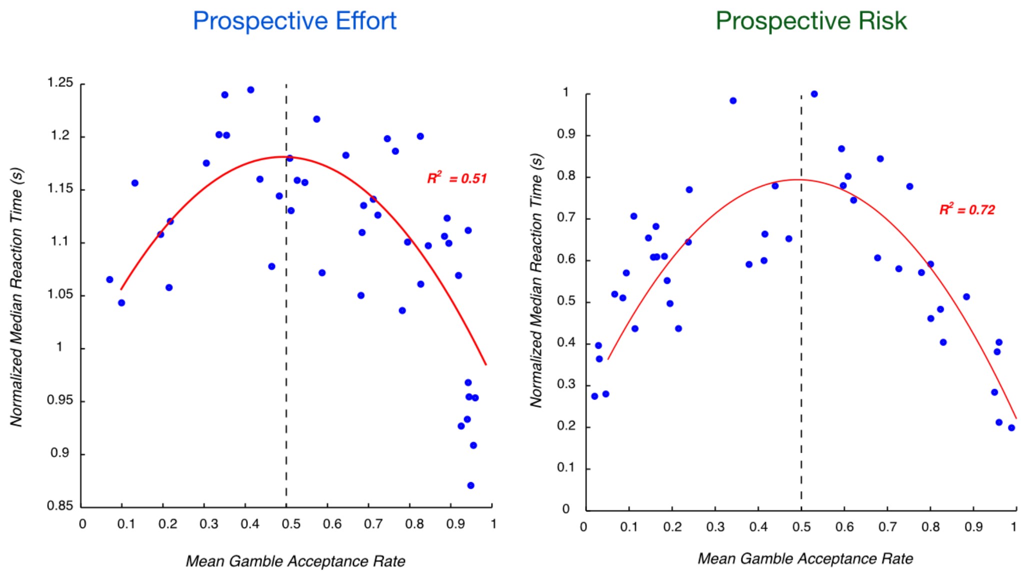

Figure 3.9: *Normalized reaction times (median-mean) plotted against average gamble acceptance rate for effort mixed gambles (left) and risk mixed gambles (right). Reaction times scaled with acceptance rate, with the slowest reaction times associated with distance from indifference. The model fit of parabolic function in red is centered at 0.5 acceptance rate.*

3.6 Neuroimaging Results: Prospective Effort Mixed Gambles

3.6.1 Whole-Brain Parametric Analysis

We first examined neuroimaging data with parametric regression analysis to identify brain regions where activity increased or decreased linearly with the magnitude of gain, loss, or effort. Our analyses focused on the time of prospective gamble choice and accounted for reaction time average within run and on a trial-by-trial basis (Mumford and Poldrack, 2014). This analysis isolated a set of regions whose activation correlated with the size of potential gain, loss and effort. The results of this analysis are summarized in table 3.1 and figure 3.10. All statistical analyses presented survived whole-brain cluster correction at a significance threshold of $p < 0.05$. The gain-responsive network included several regions previously related to anticipation and receipt of primary and secondary rewards. We found increased activation for increasing gains within vmPFC, frontal pole, striatum, and posterior cingulate cortex, as well as supplementary motor areas and right primary somatosensory and motor cortex, ipsilateral to effort production. We found decreasing activity within the left dorsolateral frontal cortex. The loss-responsive network included areas previously unreported in mixed-gamble studies. This network increased activation with the size of potential losses and included right dorsolateral PFC, frontal pole, inferior parietal lobule, primary motor and somatosensory cortex, and superior frontal gyrus in the vicinity of the cingulate motor area hand representation. Finally, the effort-responsive network included regions that increased or decreased with the magnitude of prospective effort present at choice. This network included increasing activation in left anterior insula and decreasing activation in right somatosensory and motor cortex.

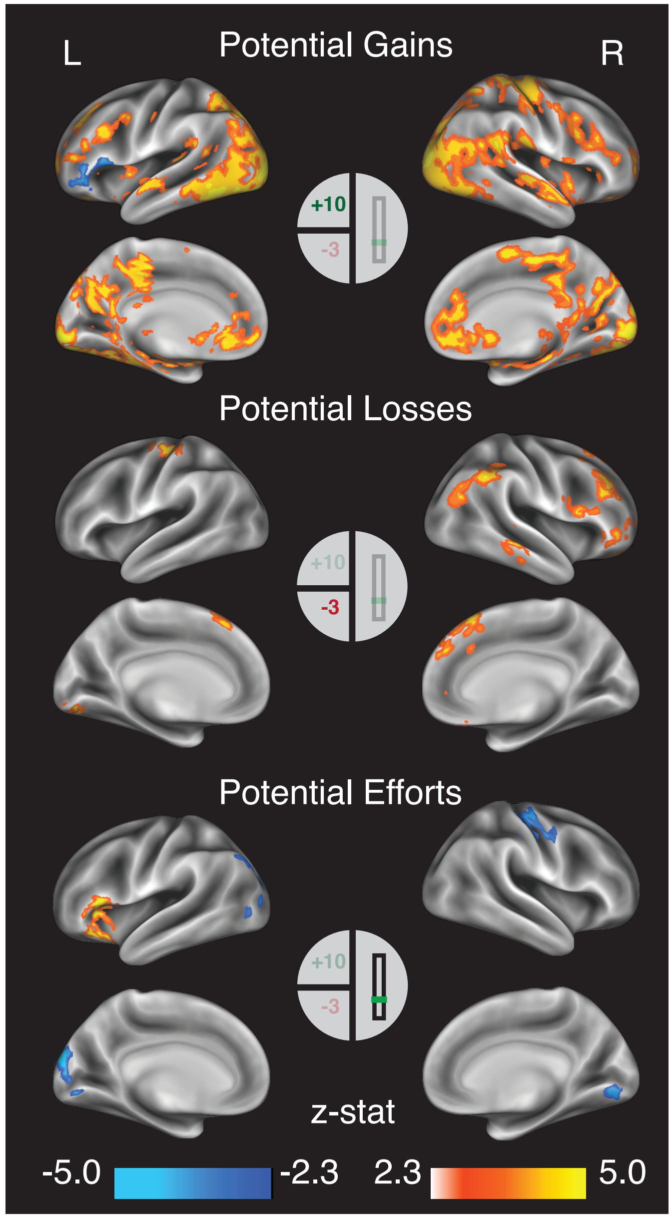

Figure 3.10: *Whole-brain analysis of parametric responses to size of potential gain (top), loss (middle) and effort (bottom). Statistical maps are projected onto an average cortical surface by multifiducial mapping in CARET software. All statistical maps were corrected for multiple comparisons at the whole-brain level by means of cluster-based Guassian random field theory in FSL at $p < 0.05$. L, left hemisphere; R, right hemisphere*

Harvard-Oxford Atlas Structural Label	L/R	extent (voxels)	MNI peak coordinates	*z-stat*
			x y z	
Increasing activation for increasing gains				
Superior frontal gyrus, Middle frontal gyrus,	Left	1171	-24 32 28	4.08
Occipital pole	Bilateral	37794	14 -96 4	5.49
Posterior cingulate cortex	Right		4 -24 48	5.4
Frontal pole	Right		24 36 -12	4.76
Medial frontal cortex	Bilateral		6 42 -6	4.21
Precentral gyrus, postcentral gyrus	Right		34 -26 64	4.08
Caudate	Right		8 8 -2	3.9
Increasing activation for increasing losses				
Frontopolar cortex	Right	312	20 42 -14	4.29
Inferior parietal lobule	Right	679	58 -50 42	4.28
Superior frontal gyrus	Bilateral	901	8 26 60	4.17
Precentral gyrus, postcentral gyrus	Left	514	-34 -30 48	4.06
Occipital fusiform gyrus	Left	474	-18 -84 -8	3.77
Middle temporal gyrus	Right	318	54 -28 -8	3.56
Middle frontal gyrus	Right	661	42 28 30	3.38
Increasing activation for increasing efforts				
Anterior insula, inferior frontal gyrus, frontal operculum cortex	Left	641	-56 22 2	3.97
Decreasing activation for increasing gains				
Inferior frontal gyrus, frontal operculum cortex, frontal pole	Left	539	-46 36 -12	3.5
Decreasing activation for increasing efforts				
Occipital pole, lateral occipital cortex	Left	855	-14 -92 20	4.32
Precentral gyrus, postcentral gyrus	Right	527	34 -24 50	3.18

Table 3.1: *Regions showing significant increasing activation or deactivation according to the size of the prospective gain, loss or effort on offer. The table includes main clusters and the Harvard-Oxford atlas labels that correspond to the location of the peak voxel. Peak voxel listed at x-y-z location in MNI space.*

In our second parametric regression analysis, we identified brain regions where activity increased or decreased linearly with a subjective value model prediction. Again, our analyses focused on the time of prospective gamble choice and accounted for reaction time average within run and on a trial-by-trial basis (Mumford and Poldrack, 2014). The results of this analysis are summarized in table 3.2 and figure 3.11. All statistical analyses presented survived whole-brain cluster correction at a significance threshold of p <0.05.

The increasing with subjective value network included several regions previously related to anticipation and receipt of primary and secondary rewards. We found increased activation for increasing subjective value within vmPFC, frontal pole, striatum, and posterior cingulate cortex, as well as supplementary motor areas and right primary sensory and motor cortex. We found decreasing activity for increasing subjective value within bilateral dorsal frontal cortex, including premotor areas, as well as left lateral prefrontal cortex, right posterior parietal cortex and primary left motor cortex.

A similar analysis examined activation related to subjective value prediction in the probability mixed gambles task. The results of this analysis are summarized in table 3.2 and figure 3.11. All statistical analyses presented survived whole-brain cluster correction at a significance threshold of $p < 0.05$. This analysis revealed only significant activation for increasing subjective value, within a broad network of visual and motor regions, as well as bilateral cingulate and medial frontal cortex.

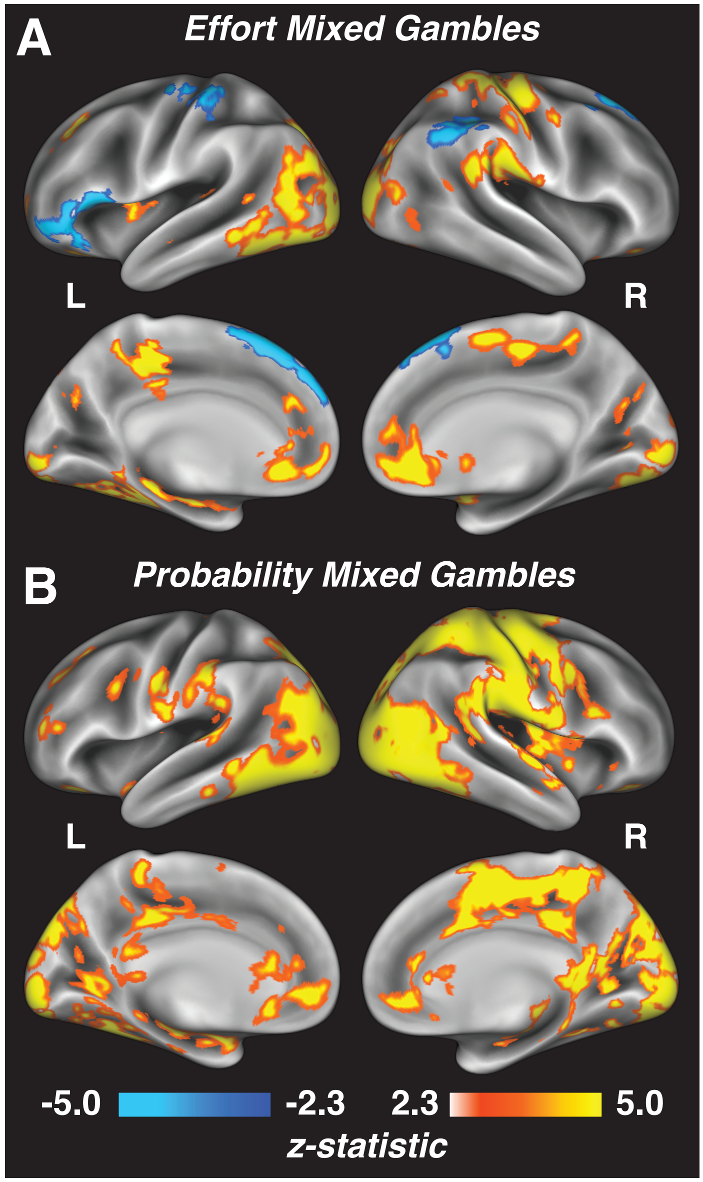

Figure 3.11: *Whole-brain analysis of parametric responses to size predicted subjective value for each gamble. Statistical maps are projected onto an average cortical surface by multifiducial mapping in CARET software. All statistical maps were corrected for multiple comparisons at the whole-brain level by means of cluster-based Guassian random field theory in FSL at $p < 0.05$. L, left hemisphere; R, right hemisphere*

Harvard-Oxford Atlas Structural Label	L/R	extent (voxels)	MNI peak coordinates	*z-stat*
			x y z	
Increasing activation for increasing subjective value				
Lateral occipital cortex, posterior temporal cortex	Left	5726	-46 -52 4	5.49
Occipital cortex	Right	2528	22 -94 6	4.64
Posterior cingulate gyrus	Right	2348	24 36 -12	4.99
Medial frontal cortex	Bilateral	1665	4 44 -10	4.61
Supramarginal gyrus, posterior division	Right	803	56 -42 22	4.26
Accumbens	Right	524	10 10 -4	4.03
Cingulate gyrus, posterior division	Left	454	-14 -32 40	4.28
Paracingulate gyrus	Left	411	-12 36 26	3.57
Decreasing activation for increasing subjective value				
Superior frontal gyrus	Bilateral	1489	10 28 62	5.03
Frontal pole	Left	880	-44 50 -8	3.94
Angular gyrus	Right	509	40 -40 40	3.30
Postcentral gyrus	Left	431	-46 -30 56	3.47

Table 3.2: *Regions showing significant increasing activation or deactivation according to the size of the subjective value estimate. The table includes main clusters and the Harvard-Oxford atlas labels that correspond to the location of the peak voxel. Peak voxel listed at x-y-z location in MNI space.*

3.6.2 Anatomical Region of Interest Analysis

We next investigated whether activity within anatomical regions previously reported in effort-based valuation studies related to our parametric regressors. We separately constrained our parametric analysis to anatomical regions of interest (ROIs) defined by the Harvard-Oxford Anatomical Atlas. These regions included (1) frontal medial cortex, (2) a combined cingulate-frontal mask of juxtapositional lobule cortex (SMA), cingulate cortex (anterior division), superior frontal gyrus and paracingulate gyrus, and (3) a somatomotor mask of combined precentral gyrus and postcentral gyrus. The anatomical location of these ROIs is illustated in figure 3.12. The results of this analysis are summarized in table 3.3. We found additional regions that did not survive cluster correction in the whole-brain analysis. Increasing gain and loss activation clusters were present in all three anatomical ROIs, cluster size corrected at $p < 0.05$. Increasing effort activation clusters were present within the combined cingulate-frontal anatomical somatomotor ROIs. We found decreasing gain activation within the cingulate-frontal and somatomotor ROIs and decreasing effort activation within frontal medial cortex and the cingulate-frontal ROI. These spatial overlap of these clusters was examined in a conjunction analysis described below.

Region of interest	L/R	extent (voxels)	MNI peak coordinates			*z-stat*
			x	y	z	
Increasing activation for increasing gains						
Frontal medial cortex	Bilateral	452	6	42	-8	4.11
Combined SMA, ACC, SFG, PCG	Bilateral	253	4	16	28	4.21
	Bilateral	222	2	-4	62	3.51
Combined precentral gyrus, postcentral gyrus	Bilateral	3272	8	-22	50	4.93
	Right		36	-22	46	3.89
Increasing activation for increasing losses						
Frontal medial cortex	Right	102	14	44	-12	3.6
Combined SMA, ACC, SFG, PCG	Bilateral	778	8	26	60	4.17
Combined precentral gyrus, postcentral gyrus	Left	501	-34	-30	48	4.06
Increasing activation for increasing efforts						
Combined SMA, ACC, SFG, PCG	Bilateral	307	-6	6	72	3.61
Combined precentral gyrus, postcentral gyrus	Left	326	-44	-30	54	3.28
Decreasing activation for increasing gains						
Combined SMA, ACC, SFG, PCG	Left	262	-8	22	56	3.55
	Right	222	16	28	58	4.62
Decreasing activation for increasing efforts						
Frontal medial cortex	Bilateral	84	-4	44	-12	3.08
Combined precentral gyrus, postcentral gyrus	Right	526	34	-24	50	3.18

Table 3.3: *Regions showing significant increasing activation or deactivation according to the size of the prospective gain, loss or effort on offer. The table includes main clusters and the Harvard-Oxford atlas labels that correspond to the location of the peak voxel: ACC, Anterior cingulate gyrus; PCG, paracingulate gyrus; SMA,supplementary motor area; SFG, superior frontal gyrus. Peak voxels listed at x-y-z location in MNI space.*

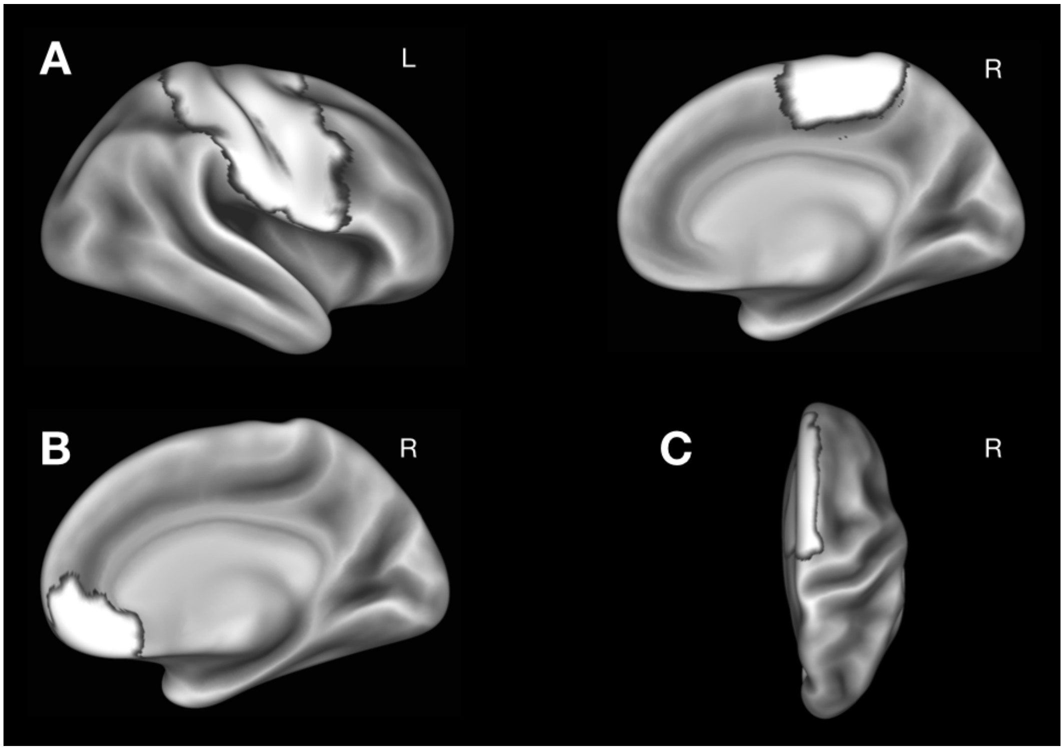

Figure 3.12: *Anatomical ROIs used for secondary parametric regression analysis. (A) somatomotor mask of combined precentral gyrus and postcentral gyrus, (B) frontal medial cortex and (C) combined cingulate-frontal mask of juxtapositional lobule cortex (SMA), cingulate cortex (anterior division), superior frontal gyrus and paracingulate gyrus. ROI masks are projected onto an average cortical surface by multifiducial mapping in CARET software. L, left hemisphere; R, right hemisphere*

3.6.3 Anatomical Region of Interest Conjunction Analyses

We performed conjunction analyses on the statistical maps obtained in the anatomical region of interest analysis to search for brain regions in which activity during choice correlated with two or more of our parametric regressors. Table 3.4 summarizes the results of this analysis. Within frontal medial cortex, we found a conjunction between increasing activity for increasing potential gains and decreasing activity for increasing prospective effort, illustrated in figure 3.13.

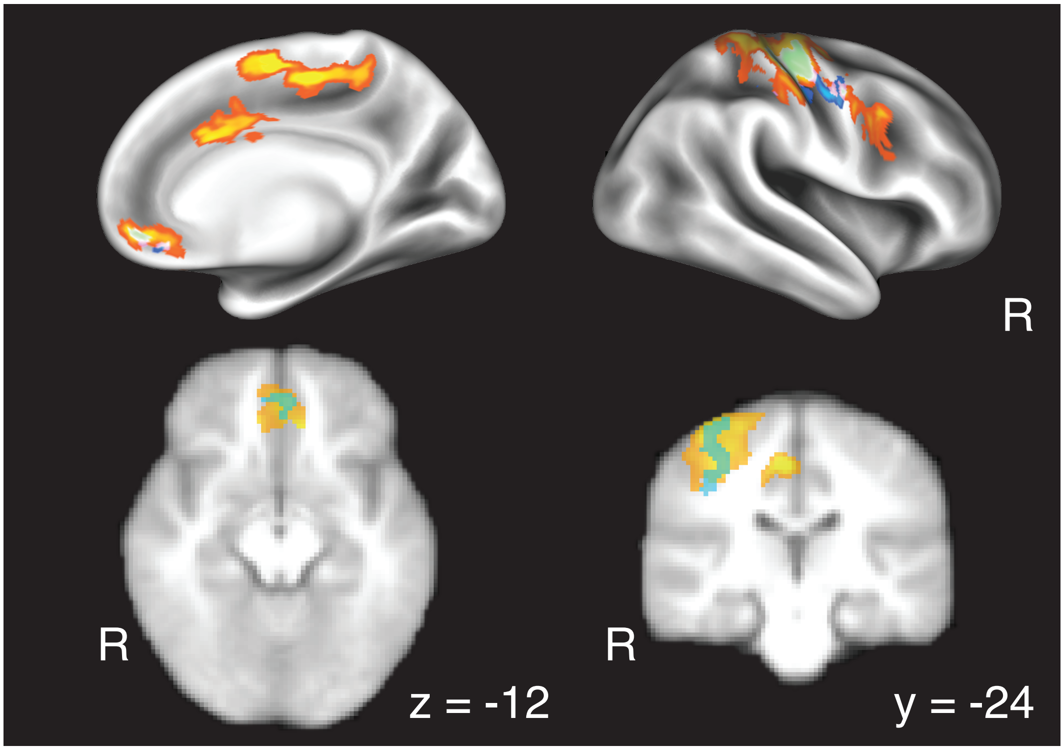

Figure 3.13: *Parametric analyses within anatomical ROIs revealed a conjunction between sensitivity for gain and effort within medial frontal cortex (left) and right somatomotor cortex. Within ROI statistical maps are projected onto an average cortical surface by multifiducial mapping in CARET software. L, left hemisphere; R, right hemisphere*

Within the somatomotor cortex mask, we found a conjunction between increasing activation for increasing gains and deactivation for increasing efforts in the right hemisphere, and increasing activation for both increasing gain and effort in the left hemisphere. Within the cingulate-frontal mask, we observed a bilateral three-way conjunction between aversive components of mixed gambles in premotor cortex: increasing activation for effort and loss and decreasing activation for increasing gain. See figure 3.14 for reference. All clusters entered into conjunction analyses were cluster size corrected at p <0.05 within their respective anatomical ROI masks.

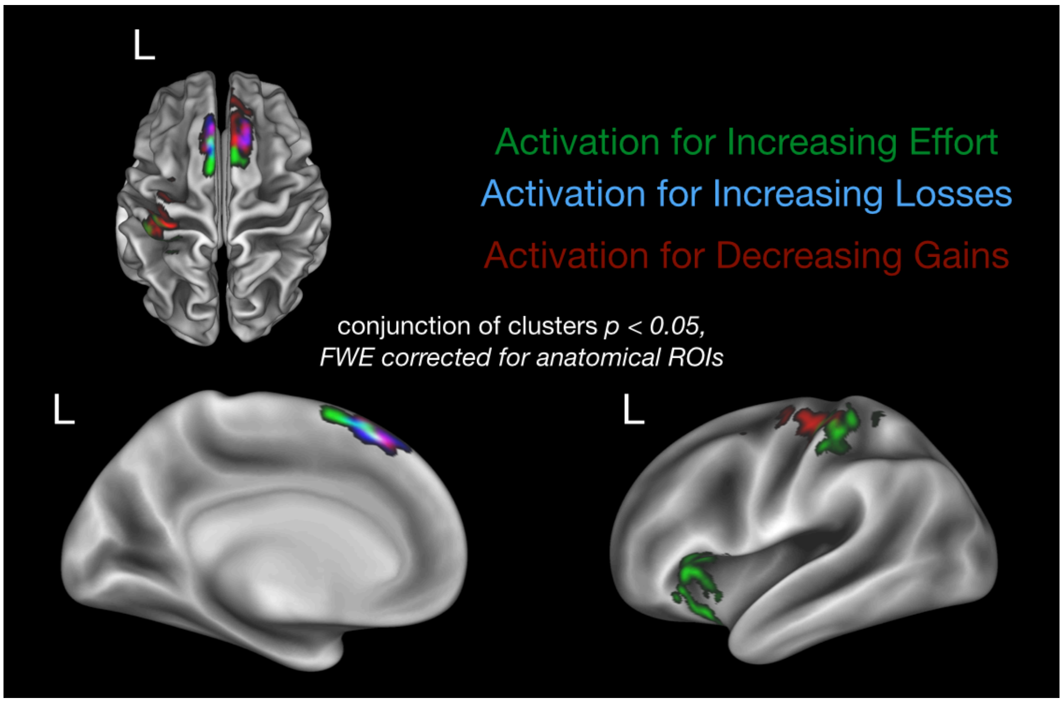

Figure 3.14: *Parametric analyses within anatomical ROIs revealed a three-way conjunction between sensitivity for gain, loss and effort within bilateral premotor cortex. Within ROI statistical maps are projected onto an average cortical surface by multifiducial mapping in CARET software. L, left hemisphere*

Harvard-Oxford Atlas Structural Label	L/R	extent (voxels)	MNI peak coordinates			*z-stat*
			x	y	z	
Increasing activation for gains, decreasing activation for efforts						
Postcentral gyrus, postcentral gyrus	Right	344	34	-24	50	3.18
Frontal medial cortex	Bilateral	65	-2	44	-12	3.05
Increasing activation for losses, decreasing activation for gains						
Superior frontal gyrus	Left	94	-6	24	58	3.54
Superior frontal gyrus	Right	96	12	24	58	3.53
Increasing activation for losses, increasing activation for efforts						
Precentral gyrus, postcentral gyrus	Left	95	-42	-30	56	3
Superior frontal gyrus	Left	24	-4	26	56	2.85
Increasing activation for efforts, decreasing activation for gains						
Superior frontal gyrus	Left	62	-8	22	62	2.84
Increasing activation for efforts, decreasing activation for gains						
Superior frontal gyrus	Left	62	-8	22	62	2.84

Table 3.4: *Regions conjointly significantly increasing activation or deactivation according to the size of the prospective gain, loss or effort on offer. Within ROI statistical maps are projected onto an average cortical surface by multifiducial mapping in CARET software. L, left hemisphere*

3.6.4 Foci of Previous Effort-Based Valuation Studies

We also tested for parametric effects of gain, loss or effort within spherical rois created at foci of peak activation in previous valuation neuroimaging studies relevant to our behavioral paradigm. Table 3.5 summarizes the results of this analysis. We performed one-tailed t-tests of all subjects mean parameter estimate within each ROI, false discovery rate corrected for multiple comparisons. Of the nine ROIs tested, only the vmPFC ROI of (Tom et al., 2007) survived a statistical of p <0.05.

Region of interest	L/R	ROI extent (voxels)	MNI coordinates	mean parameter etimate	*t*-stat	*p*-value (*FDR* corrected)
			x y z			
Activation for potential gains						
Canessa (2013) - Caudate Nucleus	Bilateral	514	-14 14 10 18 18 2	1.07	1.89	0.189
Tom (2007) vmPFC	Left	257	-6 38 -10	3.13	3.48	0.009
Activation for potential losses						
Canessa (2013) - Insular cortex	Bilateral	514	-36 -14 10 36 -28 18	0.36	0.39	0.789
Canessa (2014) - Amygdala	Right	257	28 2 -10	0.73	0.55	0.75
Activation for prospective effort						
Burke (2013) - Frontopolar cortex	Left	257	-9 62 22	0.48	0.24	0.814
Croxson (2009) - ACC	Left	257	-12 28 14	-1.82	-2.17	0.162
Prvost (2010) - ACC	Right	257	6 24 28	3.01	1.51	0.306
Burke (2013) - SMA (L)	Left	257	-9 8 52	1.43	1.02	0.561
Kurniawan (2013) - SMA	Left	257	-6 -7 64	1.2	0.65	0.751

Table 3.5: *Regions showing significant increasing activation or deactivation according to the size of the prospective gain, loss or effort on offer. The table includes main clusters and the Harvard-Oxford atlas labels that correspond to the location of the peak voxel. Peak voxel listed at x-y-z location in MNI space.*

3.6.5 Anatomical Region of Interest Conjunction Matrix Analysis

To illustrate the sensitivity to expected value within brain regions identified with whole-brain analysis, we examined overall task evoked responses and average parametric effort responses to combinations of gain and loss across all levels of effort within the five regions present in our anatomical conjunction analysis: vmPFC, left and right premotor cortex, left and right somatomotor cortex. As illustrated in figure 3.15, each cell of each matrix represents the average evoked response within the ROI for a combination of potential gain and loss trials across all subjects. Within vmPFC, we found a pattern of increased average evoked response as the size of expected value increased. We also found patterns of average evoked response sensitive for potential gains, but not losses within the somatomotor ROIs. The average parametric effort response patterns exhibited less sensitivity to expected value across the matrix, with a weak pattern of increased activation for increasing gains in left and right premotor cortex.

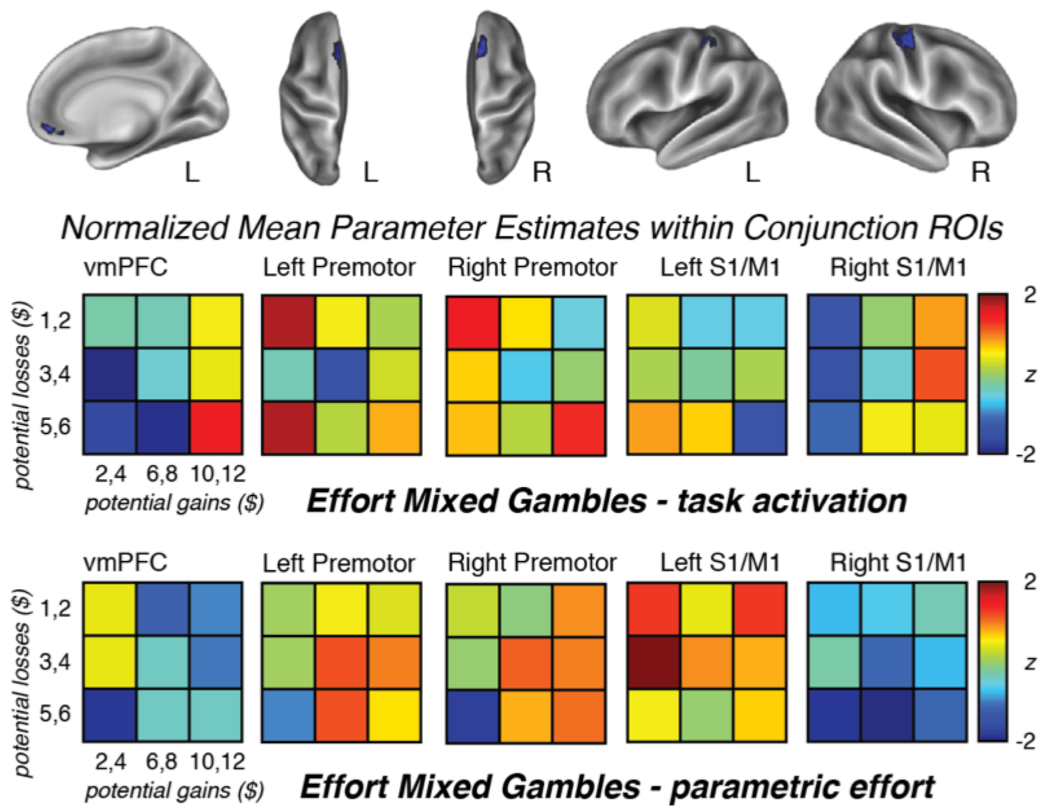

Figure 3.15: *Average task evoked response and average parametric effort response for 9 combinations of potential gain and loss were estimated within five ROIs present in conjunction analysis. Blue regions indicate location of ROIs projected onto an average cortical surface by multifiducial mapping in CARET software. Heatmaps depict average evoked response (z-scored) to combinations of gain and loss within each ROI. L, left hemisphere; R, right hemisphere*

3.7 Neuroimaging Results: Prospective Risk Mixed Gambles

We similarly examined neuroimaging data from the prospective risk phase with parametric regression analysis to identify brain regions where activity increased or decreased linearly with the magnitude of gain, loss, or risk. Our analyses focused on the time of prospective gamble choice and accounted for reaction time average within run and on a trial-by-trial basis (Mumford and Poldrack, 2014). This analysis isolated a set of regions whose activation correlated with the size of potential gain, loss and risk. Figure 3.16 illustrates the results of this analysis. All statistical maps were cluster corrected at a significance threshold of p <0.05. Unlike the prospective effort mixed gambles task, gain-responsive network included only a small region of vmPFC. Instead, the gain-responsive network included bilateral caudate, cingulate cortex, dlPFC, as well as supplementary motor areas and right primary somatosensory and motor cortex, ipsilateral somatomotor areas. The loss-responsive network consisted of only left anterior insula cortex and posterior temporal cortex. The risk-responsive network included extensive regions of bilateral somatomotor cortex, cingulate cortex and vmPFC.

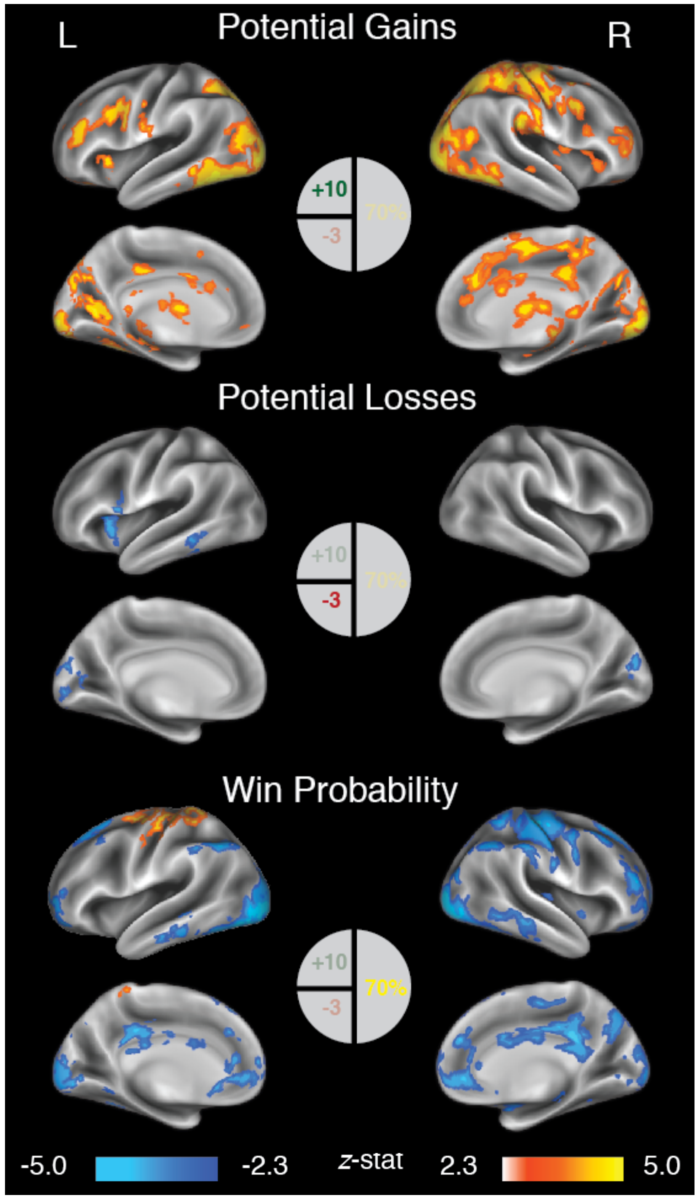

Figure 3.16: *Whole-brain analysis of parametric responses to size of potential gain (top), loss (middle) and risk (bottom). Statistical maps are projected onto an average cortical surface by multifiducial mapping in CARET software. All statistical maps were corrected for multiple comparisons at the whole-brain level by means of cluster-based Guassian random field theory in FSL at $p < 0.05$. L, left hemisphere; R, right hemisphere*

3.8 Multivariate Decoding of Prospective Effort Cost

Whole-brain support vector regression analyses within subject and across subjects was not able to predict prospective effort level at choice greater than chance with a linear support vector regression (SVR) analysis. As depicted in figure 3.17, predicted labels did not accurately label the level of prospective effort present at choice and the correlation between each subject's SVR estimates and true effort level labels was not greater than chance.

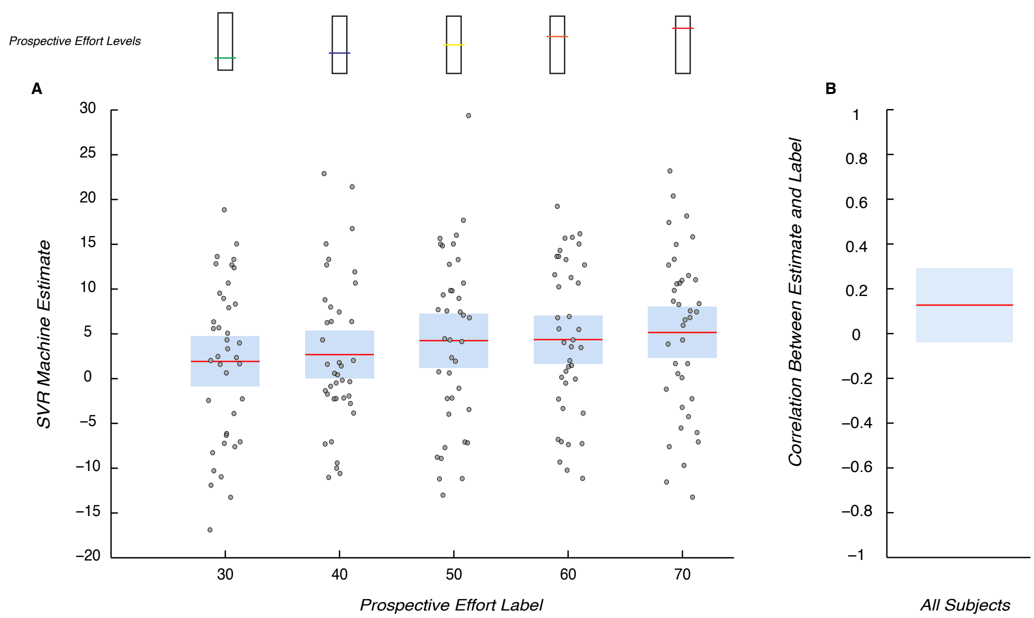

Figure 3.17: *Whole-brain analysis support vector regression analyses failed to accurately label the level of prospective effort present at choice. Red lines indicate average predictions for each level of effort. Gray circles depict each subject's left out label prediction. Shaded areas indicate standard error of the mean.*

3.9 Discussion

We report novel evidence for modulation of behavioral and neural correlates of value by prospective effort, a construct of action cost separated from production. We asked subjects to decide whether to risk performing a previously trained level of physical effort in order to resolve a monetary mixed-gamlbe. In the absence of immediate effort anticipation, we found that activity in a network of motor-related cortical areas reflected conjoint sensitivity to potential outcomes and action costs. Additionally, activity within medial frontal cortex generally regarded to reflect subjective value at choice related to both increasing expected value and effort cost, a pattern akin to a neural signal for discounted value. We confirm the involvement of prospective effort in the neural estimation of value, a common aspect of decision making in a dynamic world.

Prospective Effort Reflects a Cost in Valuation Consistent with previous effort-based valuation studies in humans and animal populations, we found that subjects choices and neural activity reflect a discounting of value by effort (Croxson et al., 2009; Prevost et al., 2010; Kurniawan et al., 2013; Burke et al., 2013). In addition to reducing subjects' willingness to take risk for rewards, prospective effort costs increased subjects sensitivity to losses over equivalent gains. Neural activity during choice reflected conjoint sensitivity to expected value and prospective effort cost, reflected in modulation of BOLD signals within medial frontal cortex, a region implicated as the locus of abstract subjective value estimates necessary for decision making among alternatives with multiple attributes (Rangel and Hare, 2010; Padoa-Schioppa and Cai, 2011; Wallis and Kennerley, 2011).

Prospective Effort-Based Decision Making Recruits Brain Regions Related to Action Selection and Production Studies of valuation processes in humans and animals consistently identify a network of frontal dompaminergic regions, including striatum, anterior cingulate cortex and vmPFC. These studies suggest that within this broad network, striatum, ACC and orbital frontal cortex may selectively process information related to decision processes under effort or delay, (Walton et al., 2006; Rushworth et al., 2007; Prevost et al., 2010). However, recent studies suggest that relationship between these regions and effort-based valuation may reflect task-specific demands, rather than a general decision making role (Euston, 2014). For example, effort-based valuation studies often confound effort cost with anticipation or delay to outcome incurred by effort exertion. Similarly confounding the interpretation of ACC in these tasks, a recent review found a strong relationship between reports of ACC activation and several correlates of choice difficulty (Shenhav et al., 2014). Furthermore, previous neuroimaging studies inconsistently report effort-based activation as ACC-related, often including dorsal premotor areas shown to contain neurons sensitive to action valuation and execution in animal models (Cowen et al., 2012; Hosokawa et al., 2013). Our parametric regression analysis did not reveal a modulation of activity within ACC by prospective effort, even when the analysis was restricted to an anatomical mask or foci of previously reported effort-responsive activations.

Instead, we found conjoint sensitivity to effort, gain and loss within dorsal supplementary motor areas, consistent with their proposed role in the integration of action planning and expected outcomes. We found additional spatially distinct encoding of prospective effort in anterior insula cortex, a region separately related to risk and effort in previous mixed gamble and effort-based valuation studies (Canessa et al., 2013; Burke et al., 2013). Intriguingly, this conjoint activity pattern follows the predictions of the affordance competition hypothesis (Cisek, 2012) whereby activity within structures related to action selection should reflect expected outcome, even without immediate action production. Similarly, our subjective value prediction analysis found a network of striatum, sensory motor, medial frontal and dorsal premotor regions related to effort-based valuation. As discussed in Chapter 5, our results notably follow previous effort-based tasks that presented choices in not reporting significant involvement of ACC in effort-based valuation (Kurniawan et al., 2013; Schouppe et al., 2014). Additional analysis of model-based expected value may further resolve the contribution of cingulate and motor regions in our prospective effort task.

A Novel Nudge for Understanding Motivated Behavior In summary, our results provide a novel perspective on effort-based valuation in the human brain. Our data suggest the relationship of the regions previously related to effort-based valuation may reflect more complex task demands than previous addressed. We extend previous findings of valuation under risk and s found that the addition of prospective effort costs recruits neural structures for action selection and production and regions related to subjective value in prefrontal cortex and striatum. Separate encoding of costs in effort-based choice may have evolved from pressure to weigh decision costs differently. Extension of prospective effort to naturalistic tasks may provide additional evidence for neural substrates of decision costs to inform models of impulsivity and anhedonia, common traits of disordered cognitive processing.

Chapter 4

Prospective Effort and Intertemporal Choice

4.1 Chapter Summary

Intertemporal choice describes decision making between two or more options whose outcomes differ in the time at which they will occur. Decisions about of the future consequences of present actions comprise a fundamental type of valuation. As reviewed in Chapter 1, behavioral and neural evidence suggests that delay-based valuation reflects a process of discounting future outcomes over immediate ones. The commonality of neural systems for intertemporal choice and effort-based valuation remains unclear. Critically, limited accounts of effort-based decision making typically utilize effort paradigms that incur delays to action or outcome, a confound that remains largely unaccounted for in human studies. This chapter describes two similar experiments designed to extend the prospective effort paradigm in the domain of intertemporal choice. We hypothesized that prospective effort challenges paired with intertemporal choices in a dual-task paradigm would parametrically alter subjects' preferences for delayed rewards. Following the prospective effort calibration and training phases described in Chapter 2, we assessed baseline temporal discounting rates in healthy subjects. We then asked them to make a second set of intertemporal choices associated with a separately resolved prospective effort challenge. Overall, subjects' discount preferences were not modulated by the level of prospective effort paired with intertemporal choices. Finally, I discuss our results with emphasis upon new potential directions and limitations of the prospective effort paradigm in this domain.

4.2 Introduction

Adaptive decision making necessitates a valuation process to select among potential options on the basis of their potential costs and benefits. Theoretical and experimental accounts suggest that this process links value to alternatives under consideration according to internally generated estimates of expected outcomes, reflected in behavioral and neural correlates of value. This approach provides the basis of understanding intertemporal choice, common decisions among alternatives that differ in the delay to their outcome. Extensive work in economics and behavioral psychology describes that when faced with intertemporal choices, decision makers valuation of future options reflects a discounting process. As discussed in section 1.2.6, intertemporal choice studies generally offer subjects a series of binary alternatives, smaller sooner (SS) or larger later (LL) prospects. Choice behavior in this task enters a regression model, whereby indifference points between SS and LL options fit a hyperbolic function (Mazur, 1987). The estimated discount parameter k describes the hyperbolic function from this analysis and enables comparisons between experimental conditions. Finally, a single choice, randomly selected at the end of the study, provides participants their selected SS or LL prospect. In the present study, we adapted this well established method of intertemporal choice preference estimation with our prospective effort paradigm to examine it as a potential modulator of delay discounting behavior. We hypothesized that a dual-task paradigm of intertemporal choices paired with prospective effort challenges would modulate k, an estimate of individual temporal discounting preferences. I present the background and results of two studies designed to test this hypothesis below, and conclude with comments on the utility of the prospective effort paradigm in the study of intertemporal choice.

4.3 Materials and Methods

4.3.1 Participants

Two samples of healthy, right-handed subjects recruited from the University of Texas at Austin community participated in the experiment. The first sample included 23 subjects (mean age = 20.2 years, standard deviation = 1.92 years, 15 females). The second sample included 27 subjects (mean age = 21.4 years, standard deviation = 2.21 years, 19 females). Informed consent was collected prior to the experiment. All participants had normal or corrected-to-normal vision, and reported no history of psychiatric diagnoses, and neuralgic or metabolic illnesses. The Human Subjects and Institutional Review Board at the University of Texas at Austin approved all procedures.

4.3.2 Behavioral Paradigm

Stimuli and Introduction: Prior to the experiment, subjects provided informed consent and were endowed with $5 cash. Subjects were instructed that they were participating in a study about preferences between delay, work and reward . Stimulus presentation and response collection were implemented with custom MATLAB code and the Psychophysics toolbox (Brainard, 1997)

Baseline Force Measurement: First, subjects were prompted to squeeze the dynamometer with their right hand as hard as possible in five intervals of two seconds interspersed with periods of rest for two seconds. The calibration procedure was performed without feedback or incentive. The average force assessed by this procedure was considered the subject's MVC for calibration of the training and test task phases. After calibration, subjects were shown a display with real-time force feedback for demonstration purposes.

Effort Training: The effort training phase was from adapted the effort training paradigm detailed in the previous chapter and summarized in figure 3.1. This phase was designed to familiarize subjects with the difficulty of performing a range of effort levels. Subjects learned to associate color and height cues with effort levels they performed, critical for subsequent prospective effort choices. Subjects completed five blocks of effort production trials without incentive at five levels of difficulty (30, 40, 50, 60 and 70% of calibrated MVC, 80 trials from one of 5 orders optimized in preparation for event-related fMRI, 16 trials of each difficulty level.) To successfully complete a trial, subjects were required to exert force at or above the given effort level for at least 1 second within a 2 second response period. Subjects received real-time effort feedback during production and success or failure to meet effort goal feedback on a trial-by-trial basis. Additionally, subjects were told how many effort trials remained in each block, and allowed to rest between briefly between blocks.

4.3.3 Interempotral Choice: Calibration

Intertemporal Choice: Subjects were instructed to select their preferred alternative in a series of intertemporal choices. All subjects completed two sequential blocks of intertemporal choice trials: baseline k elicitation trials and intertemporal choices with prospective effort attributes.

Baseline Discount Parameter Elicitation Phase Participants made a series of decisions regarding whether they would prefer to receive a smaller amount of money immediately or a larger, variable amount of money after a variable delay. For all trials, the two payment and delay options were presented adjacent to each other on a computer monitor and subjects were instructed to press a key associated with their preferred option. The immediate amount was either $5 or $10, and the delayed option ranged from $5 to $120 at three possible delays: 30, 60 and 90 days. Based on previous literature, it was assumed that each participants pattern of discounting the value of the delayed option followed a hyperbolic curve, with the steepness of the curve described by the parameter k, with larger values of k resulting in greater discounting of delayed rewards (Mazur, 1987). Given these assumptions, the subjective value of an option followed a function of the form:

$$SV = \frac{V}{(1 + kD)}$$

where SV = the subjective value of the payment after accounting for its discounted value, V = the numerical value of the payment, k = an individuals discounting parameter, and D = the delay in days of the payment. Following this form, we calculated the indifference point of each option, where the subjective value of the delayed amount was equal to the actual value of the immediate amount. We calculated the actual value of the delayed amount (LL) given a delay and immediate amount by modulation of the hyperbolic discount formula:

$$V = SV \times (1 + kD)$$

where SV is equal to the immediate amount on any given trial. There were 48 randomized adaptive trials: 24 of two immediate values ($5 and $10), and 8 occurances of each delay (30, 60 or 90 days) for each. The initial estimate of k was set to a value of (k = 0.013), an estimate of population average intertemporal choice preferences from previous studies (Kable and Glimcher, 2007; Monterosso et al., 2007), to each of two staircases, one assigned to all immediate $5 options and a second assigned to all immediate $10 options. We adjusted adaptive staircases during this task according to a maximum likelihood estimation procedure with the QUEST toolbox in MATLAB (Watson and Pelli, 1983). A combination of k-value estimate, delay, and immediate reward amount were adjusted to determine the next delayed amount (LL) presented to each participant. The QUEST parameters were initialized as follows: starting estimate (0.013), standard deviation (.02), probability of choosing delayed (LL) option (0.5), Weibull function parameters ($\beta = 5, \delta = 0.01, \gamma = 0.01$), step size (0.001), and range of responses (1). If a participant chose the immediate amount (SS), the indifference k-value on that trial was smaller than the persons actual k-value and it was increased on the next trial. If a participant chose the delayed amount (LL), the indifference k-value was decreased on the next trial. Overall, this procedure was optimized to increase the likelihood that the staircases would converge at a stable estimate of indifference (k by the end of each 24 trial choice set. Finally, as a check of the adaptive staircase procedure, we also tested a rapid k estimation procedure from behavioral economics (Kirby et al., 1999). We interspersed our staircase trials with 27 trials with prescribed fixed indifference k-values from this method.There were nine k-values (0.005, 0.0075, 0.01, 0.02, 0.03, 0.04, 0.05, 0.075, 0.1) and two randomized trial orders. Each k-value was tested once per delay and randomly assigned to a starting value of \$5 or \$10.

Baseline Temporal Discounting Parameter Estimation: We estimated the discount parameter k with three methods prior to the prospective effort intertemporal choice phase. For each subject, two k estimates were calculated as the average of 10 steps around the the convergence point of the \$5 and \$10 SS staircases. Additionally, we calculated the k value from the fixed level estimation trials (Kirby et al., 1999). The initial set of Kirby k value was the geometric mean between each two consecutively tested k values, plus the lowest and highest k values. Each geometric mean was given a point if a participant responded consistently in trials with that k value (consistently selected LL or SS around the predicted indifference for that k level). The geometric mean with the highest point total was considered a subject's final Kirby k value. In the case of ties, the geometric mean of the top two k values was used. Finally, we calculated the arithmetic mean of the three methods ($5 staircase, $10 staircase and Kirby). This estimate was considered the calibrated baseline k level for generation of choice sets in the prospective effort intertemporal choice task. To test for consistency of parameter estimation, we also performed post-hoc analysis of all trials in the baseline estimation choice set by the logistic estimation method described in the next section.

Prospective Effort and Intertemporal Choice Task: Following the discount parameter estimate phase, subjects entered the dual-task phase, prospective effort and intertemporal choice. Similar to the elicitation phase, subjects were presented with a series of trials that offered a choice between receiving a small reward (always $5) at the end of the experimental session or a larger reward (varied) at some time in the future. In addition to the intertemporal choice display, subjects were presented with one of five calibrated levels of effort from the physical effort training session. This design presented subjects a dual-task challenge: a choice between potential immediate and delayed outcomes, associated with a separately resolved prospective effort challenge of performing a level of physical effort five times in a row successfully at the end of the task. Subjects were informed that performance on the effort challenge would result in a gain (\$5) in addition to their initial endowment or loss (\$3) from it. To encourage subjects to consider the effort challenge consistently, the prospective effort cue always proceeded the intertemporal choice display by 500 milliseconds. Subjects were informed that the effort challenge associated with the intertemporal choice randomly selected trial at the end of the experiment would be resolved as described below. Figure 4.1 illustrates the task display during the baseline temperal discounting estimation and dual-task intertemporal choice phases.

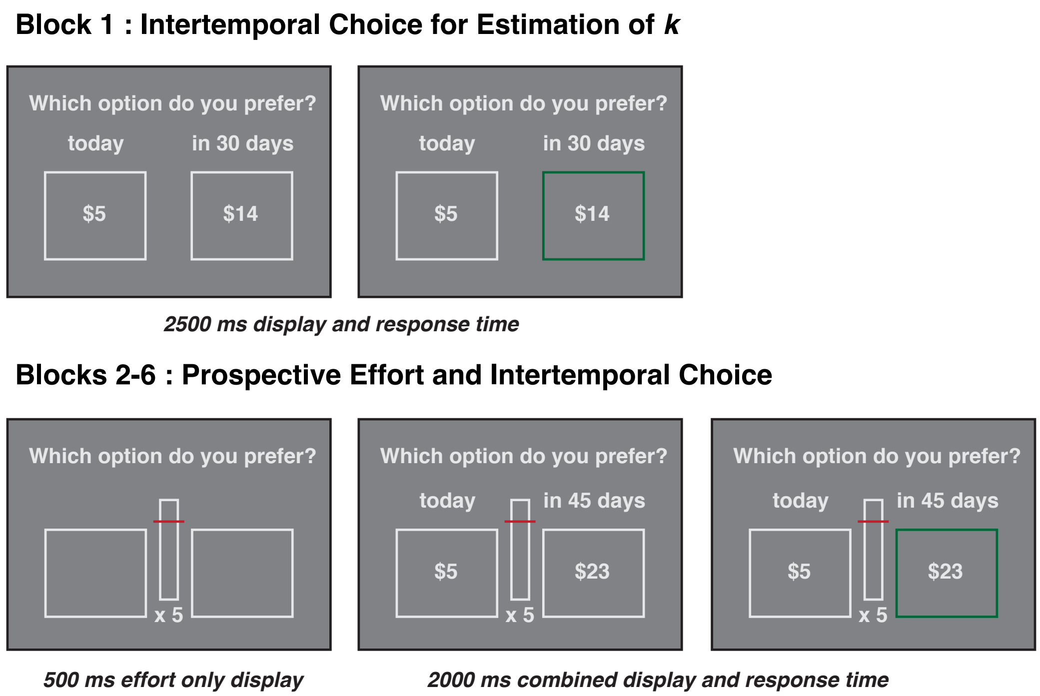

Figure 4.1: *Examples of stimulus displays during the two intertemporal choice tasks. During block 1, the discount parameter elicitation phase, subjects were presented two options and indicated their preference with a key press. In blocks 2-6, subjects were presented a series of individually calibrated intertemporal choices paired with prospective effort challenges and again indicated their preference with a key press.*

The choice set included 210 trials, split into 5 blocks of 42 trials, trial order optimized for event-related fMRI. As illustrated in 4.2, we calibrated the range of potential LL values according to the estimated k-value obtained in the baseline discount parameter estimation phase. In both samples, we tested a choice set of 42 trials, with 6 possible delays (15, 30, 45, 60, 75 or 90 days) and 7 possible k value multipliers. In each sample, we varied the amount of LL reward on offer around individual subject's estimated log-transformed k

parameter according to a parametric constant (ϵ) from $\pm$ .1, .2 or .3 $\times$ k. For each trial, the LL value presented was calculated according to the hyperbolic discounting equation: LL = SS * ((1 + (kϵ)D) . For example, if a subject's choices in intertemporal choice block 1 (see figure 4.1) resulted in an estimated k level of (0.03), LL values presented to the subject in the prospective effort intertemporal choice blocks were calculated as LL = \$5 $\times$ (1 + ($\pm\epsilon$ $\times$ 0.03) $\times$ delay) . The only difference between samples in the task concerned the rounding of LL values. In sample 1, we rounded LL values to the nearest whole dollar. In order to increase the number of unique values in the choice set (discussed further in section 4.5) we rounded LL values to the nearest \$0.25.

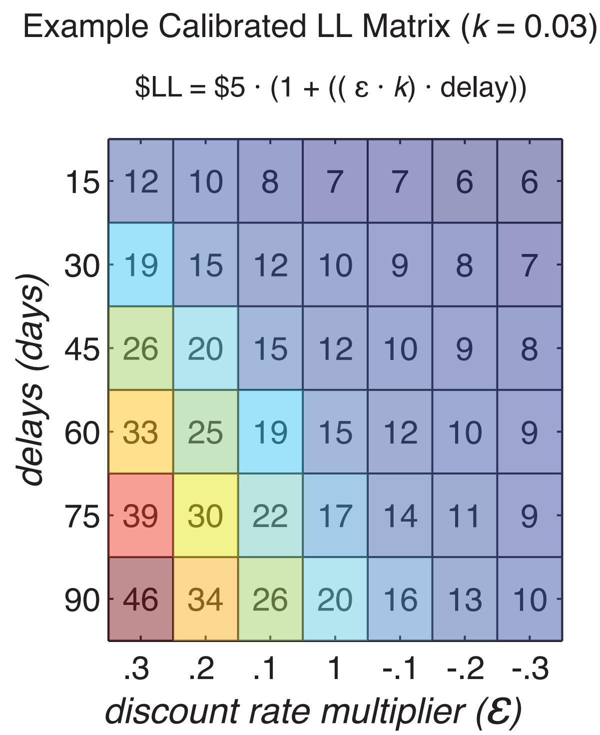

Figure 4.2: *Each subject's choice set was created according to their initial discount parameter estimate whereby their discount parameter k was multiplied by their discount rate constant ϵ . In the example shown, a subject with an initial k value estimate of 0.03 was presented a range of LL values from \$6 to \$46 at each of five levels of prospective effort in the dual-task. The range of discount rate multiplier reflects the log-transformed multiplicative increase or decrease from baseline k. 1 indicates the initial calibrated baseline k value.*

Prospective Effort Temporal Discounting Parameter Estimation We performed post-hoc analyses to estimate the discount parameter k for each subject within each prospective effort level choice set. We fit a discount function for each 42 trial choice set with a two-parameter binary logit model. The choice probabilty function followed the form:

$$p_{LL} = \frac{1}{1 + \exp(\beta(SV_{LL} - SV_{SS}))}$$

where p_{LL} represents the probability of selecting the LL option as a function of the difference between the subjective values of the SS and LL options. The parameter β represents noise, inconsistency in choice preferences. As described above, subjective values of the SS and LL options were calculated according to equation:

$$SV = V/(1 + kD)$$

where V was \$5, the constant value of the immediate option, and D was the proposed delay in days. Finally, the discount parameter k was fit by maximum likelihood estimation.

Confidence Ratings: After the mixed gambles phases and while still in the scanner, subjects were asked to rate how confident they were that they could perform each of nine levels of effort (10-90% of their MVC in 10% increments) five times in a row, as required to resolve gambles in the prospective effort phase of the experiment successfully.

Prospective Effort and Intertemporal Choice Resolution: At the end of the experiment, one trial from the prospective effort intertemporal choice session was drawn at random. Subjects received their choice (either \$5 or a calibrated LL value) in the form of an electronic *Amazon* gift card. Gift cards were issued for either immediate redemption or at the delay associated with their choice. Separately, subjects were presented with the effort challenge associated with the effort level present in the randomly selected resolution trial. The challenge comprised 5 sequential physical effort grip trials, as completed in the training phase. If the subject successfully completed their challenge, they were awarded \$5 in cash in addition to their endowment. If they were not successful, subjects paid a penalty of \$3 in cash from their endowment. Finally, subjects completed a questionnaire about their discounting preferences and the behavioral paradigm.

4.4 Behavioral Results

4.4.1 Prospective Effort Task Validation:

As in our previous experiments, subjects' performance and confidence ratings reflected a graded cost imposed by our physical grip effort paradigm. Results of the training and rating phases for each sample are summarized in 4.3 In both samples, subjects' average performance during the effort training phase reflected an effect of effort level: sample 1 ($F(4, 110) = 15.65, p < 0.001$), sample 2 ($F(4, 130) = 16, p < 0.001$). Subjects' training behavior was well described by a linear model whereby increased effort level reduced training success: sample 1 ($\beta = -0.13, t(113) = -7.84, p < 0.001$). Effort level explained a significant portion of variance in training success in sample 1 ($R^2 = 0.35, F = 61.6, p < 0.001$). We found a similar relationship in sample 2 ($\beta = -2.6, t(133) = -8.01, p < 0.001$), whereby effort level explained a significant portion of variance in training success ($R^2 = 0.32, F = 64.2, p < 0.001$).

Similarly, subjects' post-task confidence ratings reflected an effect of effort level upon expected success in the effort challenge resolution phase. Average performance during the effort training phase reflected an effect of effort level: sample 1 ($F_(8, 198) = 50.5, p < 0.001$), sample 2: ($F(8, 234) = 47.54, p < 0.001$). We found that subjects' post-task confidence ratings were well described by a linear model whereby effort level predicted confidence in sample 1: ($\beta = -9.88, t(205) = -20.17, p < 0.001$), whereby effort level explained a significant portion of variance in confidence ratings ($R^2 = 0.66, F = 407, p < 0.001$), and sample 2: ($\beta = -10.21, t(241) = -19.4, p < 0.001$) with the same model ($R^2 = 0.60F = 377, p < 0.001$).

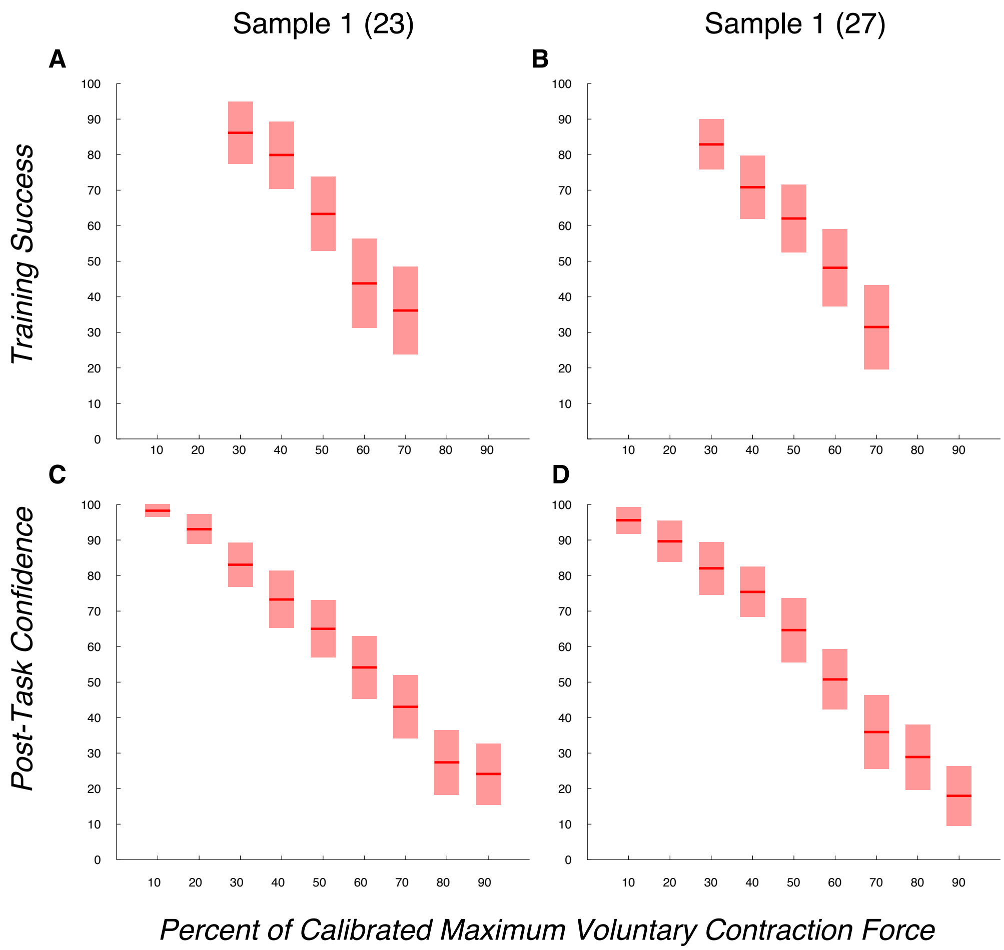

Figure 4.3: *Subjects' average effort grip force performance (A,B) and post-task confidence ratings (C,D) reflect modulation by effort level in each sample. Shaded color bars around group averages indicate standard error of the mean.*

4.4.2 Baseline Temporal Discount Parameter Estimation:

Temporal discount parameter k estimates obtained during the initial intertemporal choice phase were tested for consistency between elicitation method in each sample. Estimates of k obtained with each method were

were highly correlated within each subject in both samples ($Spearman's \rho > 0.8, p < 0.001$), see figure 4.4 for illustration of cross-method estimate correlation. Figure 4.5 illustrates consistent k estimates for two subjects, one with more impatient preferences than the other.

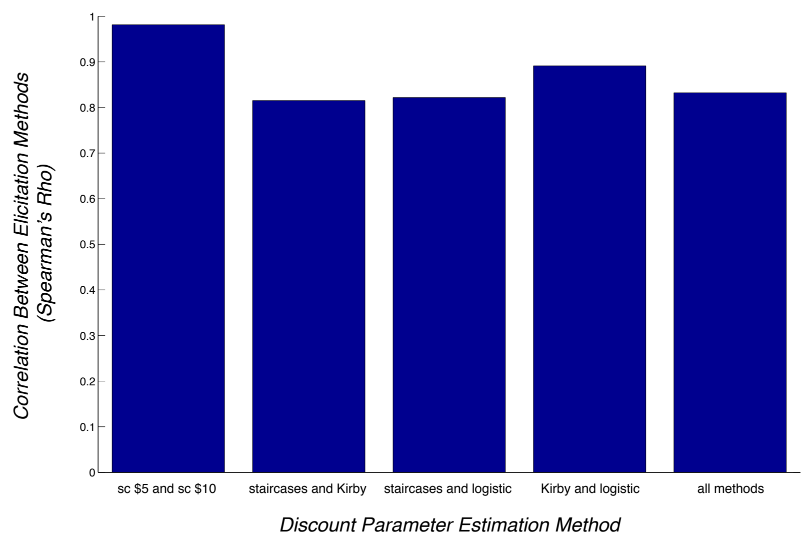

Figure 4.4: *Estimates of all individual's discount parameters by adaptive, logistic and fixed methods were highly correlated. Bars indicate Spearman's* ρ *correlation between adaptive staircases at two immediate reward values (sc5 and sc10), fixed* k *trials (Kirby, 1999) and post-hoc logistic maximum likelihood estimation methods. All methods were highly correlated:* $Spearman's\ \rho > 0.8, p < 0.001$

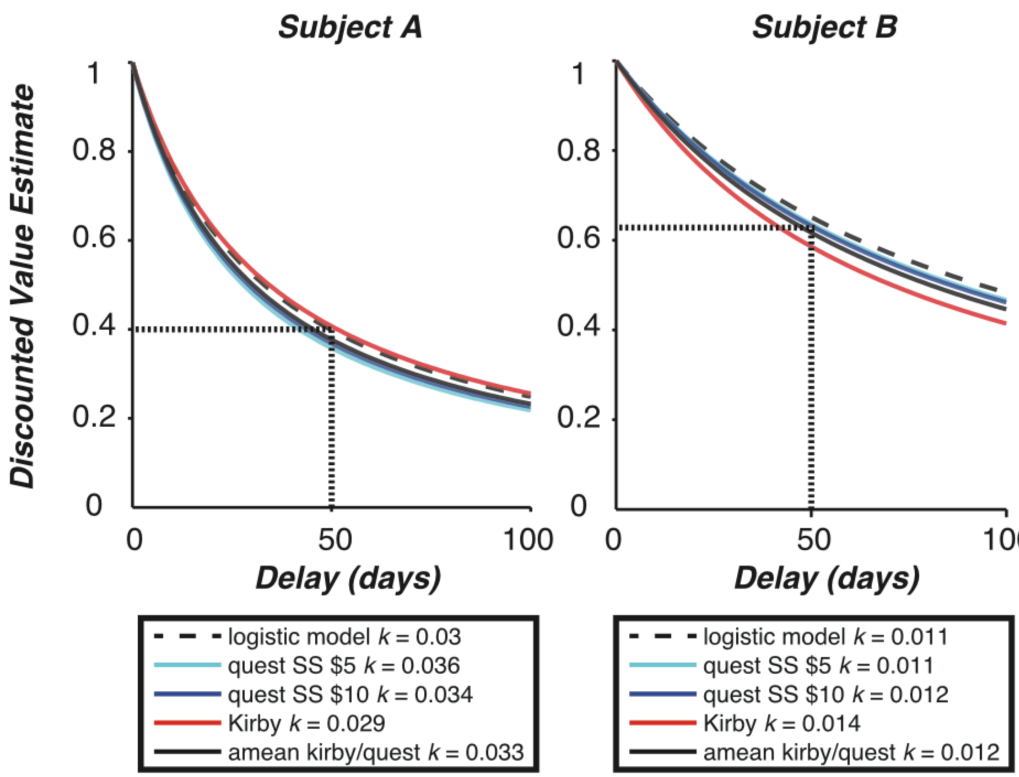

Figure 4.5: *Estimates of individual's discount parameter estimates by adaptive, logistic and fixed methods. All methods were highly correlated. At left, a subject with more impatient choice preferences, and at right, a subject with more patient discount preferences*

4.4.3 Dual-Task Intertemporal Choices

Subjects' choices during the prospective effort intertemporal choice phase did not exhibit a consistent pattern of modulation by prospective effort cost. We separately analyzed average gamble acceptance rates for each sample's data across effort conditions. In sample 1, average discount parameters were not modulated by prospective effort level ($F(4, 110) = 0.58, p = 0.69$).

The results of sample 1 are illustrated in figure 4.6.

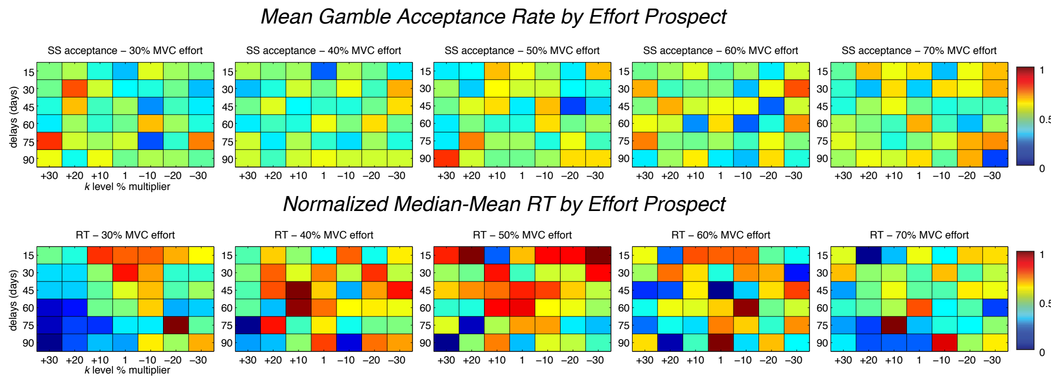

Figure 4.6: *Heatmaps illustrate average gamble acceptance rates and reaction times across each level of prospective effort. (top) Each heatmap represents the average acceptance rate for each offer, a combination of delay, discount rate multiplier and baseline k level. (bottom) Each heatmap illustrates the median-mean reaction time for each offer. Overall, average gamble behavior and reaction time were not modulated by prospective effort attributes in a dual-task.*

Similarly, we did not find a consistent pattern of discount parameter modulation by effort prospect in our second sample. The was no effect of prospective effort level upon average discount parameter estimate: $(F(4, 140) = 0.55, p = 0.7)$. A linear function did not describe estimated k parameters by effort level $(\beta = -0.61, t(143) = -0.56, p = 0.57)$. The results of the second samples' gamble behavior are illustrated in figure 4.7.

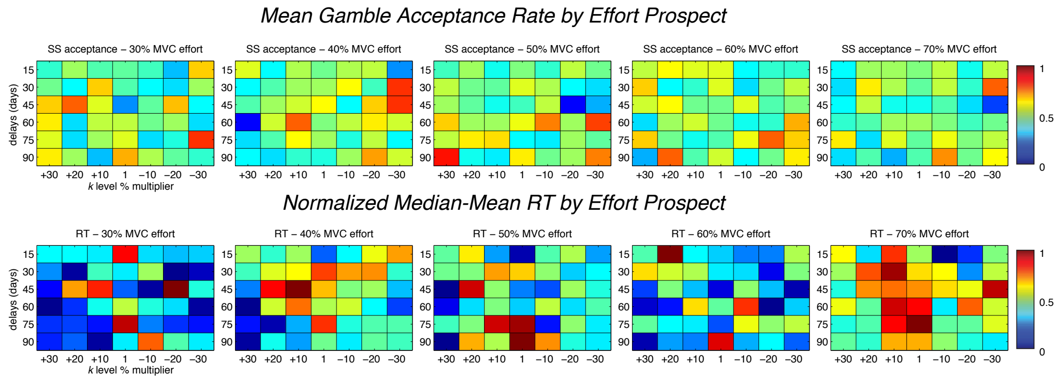

Figure 4.7: *Heatmaps illustrate average gamble acceptance rates and reaction times across each level of prospective effort. (top) Each heatmap represents the average acceptance rate for each offer, a combination of delay, discount rate multiplier and baseline k level. (bottom) Each heatmap illustrates the median-mean reaction time for each offer. Overall, average gamble behavior and reaction time were not modulated by prospective effort attributes in a dual-task.*

Finally, all subjects completed a survey after the experimental session. The results of the survey are depicted in table 4.1 below. On average, subjects indicated that they did not strongly consider the potential effort prospect during dual-task intertemporal choices.

Post-Task Survey Question (1-7)	***Mean Response***
How motivated were you during the task? Did you care about your selections? 1 = did not care much, 7 = cared a lot	4.68
How interested were you in receiving money today, compared to in the future? 1 = did not care much, 7 = cared a lot	4.26
Did you believe that we would actually issue you a gift card with the proper amount in the future? 1 = did not believe, 7 = strongly believed	5.85
How much did you think about the potential effort when making your choices? 1 = not at all, 7 = a lot	2.86

Table 4.1: *Temporal Discounting Task Survey Results*

4.5 Discussion

There exists considerable evidence that choice behavior in many species reflects discounting of delayed rewards over immediate ones. Studies of the neural basis of delay-based valuation suggest that a core network of prefrontal regions calculate the value of delayed options as a function of their distance in time. Furthermore, several studies suggest at least partial dissociation between neural correlates of delay-based valuation and other common costs (Walton et al., 2006; Prevost et al., 2010). Despite substantial progress, the influence of effort costs upon intertemporal choice behavior remains largely unexamined outside of the literature on animal foraging behavior. We hypothesized that pairing an effort prospect with an intertemporal choice would modulate subjects' preferences for immediate or delayed rewards. We adapted the prospective effort paradigm in a dual-task that asked subjects to reflect upon intertemporal choices that were associated with a prospective effort cost when resolved. Contrary to our study of prospective effort under risk, we did not observe a consistent pattern of choice behavior modulation as prospective effort level increased. Nevertheless, these experiments offer useful lessons for the integration effort-based decision making and intertemporal choice literature. Our choice sets were individually calibrated according to a baseline temporal discounting estimate, designed to present subjects intertemporal choices around their expected indifference points between delayed immediate rewards. However, our results suggest that a large, fixed choice set may improve consistency of discount parameter estimates. For example, subjects with very small estimates of baseline discounting (e.g. $k < 0.005$) were by design presented with a narrow range of unique LL values, the maximum of which might be less than twice the SS value. Consequently, these subjects exhibited substantial inconsistency in their choice behavior that made accurate estimation of their k parameter impossible. Overall, subsequent studies with small choice sets should offer fewer levels of prospective effort and/or a wider range of potential delays and discount factors. In addition to a wider choice set and improved estimation methods, modification of the prospective effort paradigm is needed as well. A post-task survey (see table 4.1 indicated that on average, subjects did not consider strongly the level of prospective effort upon their choices. Thus, the present results likely reflect well-described insensitivity to prospective costs among subjects 'playing for peanuts'. Given the relatively small loss incurred by the failure to perform prospective effort, subjects were likely motivated to consider our task in an delay-based frame alone. Modification of the paradigm to include large potential losses for failure to succeed in effort trials or other aversive contingencies may elicit different results. With these comments in mind, the prospective effort approach may yet yield new evidence for interaction or dissociation of effort and delay costs in decision making processes. In the final chapter, I will discuss broader implications of this study for future attempts to disentangle behavioral and neural correlates of valuation related to effort and delay.

Chapter 5

General Discussion

5.1 Summary

We often face decisions of whether to act, choices between alternatives that vary in inherent effort costs. When presented with such choices, adaptive behavior requires a valuation process that weighs expected costs and rewards and integrates them among alternatives to guide choice. The integration of psychological and economic theory with neural data has begun to reveal the behavioral and neural correlates of specific cost valuation processes of common choices. Compared to canonical economic costs such as risk and delay, accounts of effort-based valuation lack consensus. This thesis considered a novel prospective effort paradigm designed to separate effort-based valuation from risk and delay costs and link patterns of effort-based choice behavior and neural activity. In this final chapter, I discuss the contributions of the work presented in this thesis in the context of previous neuroeconomic research. I discuss the theoretical foundation of effort-based valuation research and summarize our findings in comparison to limited existing accounts of effort-based valuation in humans. Finally, I comment upon outstanding challenges related to the study of effort and theoretical accounts of cognition likely to inform the next generation of effort-based valuation research.

5.2 Effort-Based Valuation and the Law of Least Work

Decades of research demonstrate that normative choice behavior reflects a cost-benefit analysis whereby cost expectations weigh upon potential rewards. Like rewards, costs may take many forms, from pain, delay, and monetary loss to social exclusion. A construct of intrinsic action cost, effort describes the energetic resources required to pursue an alternative. While choice behavior research historically focused on reward centric accounts (value-maximization), century old observations and descriptions of effort-based choice support attention to avoidance of energy expenditure (effort-minimization). The basic principle of this framework, described by (Hull, 1943) as *the law of least effort*, remains relevant today. It states that all else being equal, a decision maker will select the course of action associated with the least energy expenditure. This effort-aversion principle follows similar accounts in behavioral economics that link effort to disutility, and accounts of foraging behavior in diverse species (Charnov, 1976).

5.3 Neuroimaging of Effort: Advances and Caveats

As discussed in Chapter 1, the emergence of neuroeconomics has inspired diverse attempts to link neural data to behavioral patterns described by psychological and economic theories. The contribution of contemporary neuroimaging studies of effort-based choice to neuroeconomics centers largely upon the extension of two sets of findings from the animal literature in human subjects. In the first group, several studies supported a series seminal experiments by Salamone et al. (2012, 2007) that linked dopamine and the ventral striatum, a region related to a reinforcement learning model of motivated behavior, to invigoration of effort-based behavior and cost-benefit inferences (Croxson et al., 2009; Kurniawan et al., 2010). In the second group, researchers adapted paradigms from animal literature (Rudebeck et al., 2006) to test for the separation of neural systems for effort and delay based choices, particularly the role of the anterior cingulate cortex in effort-based choices (Prevost et al., 2010). Together, these neuroimaging studies support the basic notion of effort as a cost, revealed in patterns of neural activity related to value present in striatum. Secondly, a subset of these studies reinforce the localization of effort-based valuation inferences to the ACC and frontopolar cortex, regions outside the core fronto-striatal valuation network (Prevost et al., 2010; Kurniawan et al., 2013; Burke et al., 2013). While broadly consistent previous animal studies, contemporary neuroimaging studies of effort-based valuation present several important caveats to address. Foremost, the varied task designs employed across studies consistently fail to address the critical confound of time. In both the animal and human tasks, non-choice or forced-choice scenarios fail to address confound of greater delay with greater effort exertion, as well as potential activity related to expected exertion or outcomes. Thus, the patterns of neural activity reported in these studies cannot reflect purely effort-based inferences. Notably, two recent neuroimaging studies that offered physical (Kurniawan et al., 2013) or cognitive (Schouppe et al., 2014) effort-based choices did not find significant evidence for ACC modulation by effort cost. Together with our own study, these results suggest that task demands in effort-based choice may differ substantially from those related to passive reception of cost-benefit stimuli or forced choice contexts, as shown in disparate patterns of neural activity at choice. Regardless, as discussed below, all studies to date presented highly constrained, temporally separated events that differ substantially from naturalistic choices.

5.4 Summary of Findings in Context

In our first set of studies, we adapted a mixed gamble decision making task from behavioral economics to assess the influence of prospective effort upon risk preference. In multiple behavioral studies, we found reduced willingness to take risks associated with increased prospective effort challenges (see Chapter 2). We developed this task to address a key confound in the effort-based decision making literature, a failure to separate choices about effort from immediate effort production or outcome anticipation. Our behavioral studies found that individually calibrated prospective effort conditions imposed a graded cost upon decision makers. A subsequent neuroimaging study examined neural activity during prospective effort mixed gamble choices. We found that in the absence of immediate effort production, a network of brain regions responded to prospective effort costs (see Chapter 3). These regions included those previously related to anticipation of aversive outcomes, and effort production, such as insular cortex and motor cortex (Meyniel et al., 2013; Kurniawan et al., 2013). Notably, we found novel evidence for sensitivity to prospective effort in a large region of interest that included dorsal premotor cortex. Contrary to previous effort-related animal and human neuroimaging studies, analyses performed whole-brain level and within several small volume regions of interest did not find sensitivity to effort in the anterior cingulate cortex. Similarly, we did not observe sensitivity to effort cost within the striatum, a part of the core valuation network implicated as the site of integration of outcome value and effort cost (Kurniawan et al., 2010; Schouppe et al., 2014) at choice. While our results do not dissociate specific structures from effort-based valuation, they follow recent neurophysiological findings in animal models that suggest the contribution of ACC may reflect nuanced, context specific demands (Pasquereau and Turner, 2013; Euston, 2014). For example, the findings of Euston (2014) suggest that ACC does not contribute to effort-based action selection, but provides critical input to maintain effortful behavior in spite of the cost of exertion. Similarly, recent accounts put into question the direct link of dopamine-related activity within striatum to effort and reward expectations. Specifically, a critical review of neuroeconomic literature sutggests that activation of striatum may reflect influences of salience in task designs, rather than expected cost-benefit or preferences (Salamone and Correa, 2012). Finally, we found novel evidence for neural correlates of hedonic value discounted by prospective effort cost. Many studies implicate vmPFC activity at choice as a neural correlate of abstract subjective value across many decision making contexts (Sescousse et al., 2013). We found that activity within this region reflected sensitivity to potential gains and costs as they varied across trials in our task. Our finding adds to the growing consensus that vmPFC activity at choice reflects an estimate of the cost and benefit of the chosen option, necessary for learning contingencies of actions and outcomes. In a separate analysis, we found that neural activity within a similar network of regions was sensitive to subjective value predicted by a hyperbolic effort-discounting model. Compared to a similar model of subjective value under risk prospects, this analysis again revealed the contribution of dorsal premotor areas in effort based inference. In total, our experiments regarding decision making under risk and prospective effort presented a new behavioral approach for testing hypotheses related effort-based valuation in healthy and abnormal populations and provided novel evidence of distinct neural activity patterns related to effort-based valuation. Subsequent studies described in Chapter4 attempted to apply the prospective effort paradigm to valuation of intertemporal choices. In a dual-task paradigm, we did not find modulation of individual preferences when paired with prospective effort challenges. Despite individual calibration of expected sensitivity to delay, this paradigm did not induce consistent patterns of increased or decreased preferences for immediate over delayed rewards. A post-task assessment of subjects' behavior and survey responses suggested that prospective effort attributes were not salient in subjects' dual-task choices. Nevertheless, these studies extended our original behavioral findings and contributed to further calibration and confirmation of prospective training paradigm. We found that additional calibration trials resulted in a stronger linear relationship between prospective effort level, training performance and post-task confidence. Together, the findings of our intertemporal choice and risk studies presented and validated a rapid, simple paradigm for imposition of effort cost in neuroeconomic study and suggested new directions for task design.

5.5 Outstanding Issues and Future Directions

The integration of behavioral and biological accounts of decision making processes has begun to substantially contribute to the understanding of effort-based choice behavior. As a nascent discipline, there remain several open questions likely to guide future endeavors to link effort motivated behavior to neural activity.

5.5.1 Formal Models of Effort-Based Valuation

The success of neuroeconomic accounts of valuation under delay and risk derives in large part from their ability to test specific predictions of behavioral models of valuation, for example the seminal studies of Tom et al. (2007); Kable and Glimcher (2007) described in Chapter 1. Similarly, a unified account of effort-based valuation requires the examination of model predictions and neural activity during choice. To date, accounts of effort-based decision making rely upon simple additive models of cost or borrow the hyperbolic discounting model from intertemporal choice studies (Prevost et al., 2010; Talmi and Pine, 2012). The account of the integration of effort and outcomes in our experiments presented thus far remains a largely informal description of effort-based valuation. The final account of the data presented in this thesis must formally test the predictions of valuation under multiple existing models and novel models derived from paradigm behavior, including linear, hyperbolic and parabolic effort discount functions (Bonnelle et al., 2014). Additionally, effort integration models should incorporate information related to individual subject's effort performance and confidence ratings to identify patterns of behavior and neural activity related to differences in effort preferences.

5.5.2 Naturalistic Task Design

We know that the brain evolved. This fact not only motivates descriptions of mechanisms of effort-based choice, but also constrains them with respect to the choices our ancestors faced. Critically, ethologically relevant choices incur multiple canonical economic costs simultaneously. A model of simultaneous valuation of risk, delay and effort that identifies neural correlates of each process and subjective value remains a considerable challenge. One potential approach illustrated in figure 5.1 presents subjects with a choice between costs prior to evaluation of risk preferences. However, such a constrained task differs substantially from naturalistic behavior. Similarly, while our research and much of the field derives from the assumption of anatomically modular, sequential stages of neural processing, attention must be paid to more naturalistic choice proposals. For example, the *Affordance Competition Hypothesis* posits that evolutionary pressure cannot result in a brain optimally designed to evaluate discrete, serially presented trials that comprise typical neuroeconomic studies (Cisek, 2012). Instead, the brain should prepare responses to expected affordances, potential actions associated with outcomes, and continuously update their representation with relevant cost-benefit information. The finding of neural activity related to outcome or subjective value model predictions in our neuroimaging study may reflect such neural processes. While directly testing the predictions of this model with neuroimaging present considerable design challenges, the advance of rapid acquisition technology and whole-brain pattern analysis techniques may provide the framework to link neural activity to affordance competition in more naturalistic effort-based choices.

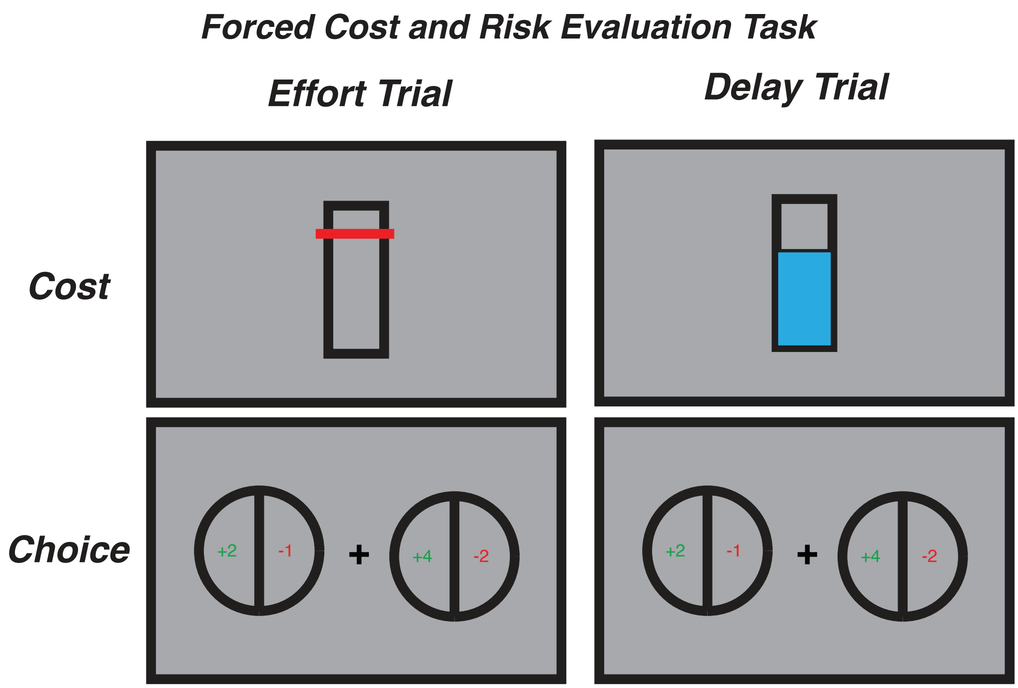

Figure 5.1: *The integration of multiple cost attributes into a single ecologically valid task remains a considerable challenge for neuroeconomic research. One approach might ask subjects to reflect upon prospective or subsequent cost type (top), prior to a choice among risk prospects (bottom).*

5.5.3 Limitations of Physical Effort Paradigms

In the work presented in this thesis, I argued that a prospective effort paradigm offers significant advantages over previous effort-based paradigms. However, modulation of effort cost by grip force production represents a specific embodied effort cost. Integration of our prospective effort account with the literature on cognitive effort, fatigue and persistence is needed to produce a complete normative account of effort cost. Unlike discrete grip force production, cognitive effort incurs highly variable temporal costs, similar to repetitive physical responding. Both forms of effort require self-control to balance temporally limited motivational demands, a concept explored in recent reviews of cognitive effort (Kurzban et al., 2013) and cingulate cortex function (Shenhav et al., 2014) that describe their relation to motivational impairments that characterize many psychological disorders.

5.5.4 Effort Justification or Effort-Based Enhancement of Value?

The development and validation of the prospective effort paradigm presented in this thesis was predicated on the assumption that physical effort reflects a cost that decreases subjective value. While there exists considerable evidence to support effort-discounting, a unified, normative account of effort-based valuation must address paradoxical reports of value boosted by effort. For example, limited reports suggest that animals exhibit enhanced preferences for cues associated with more effortful actions (Johnson and Gallagher, 2011; Klein et al., 2005). In daily life, humans and animals readily engage and persist in effortful tasks. Theoretical and experimental accounts suggest the involvement of brainstem domapinergic and noradrenergic systems in the invigoration and maintenance of effortful behaviors (Kurzban et al., 2013; Shenhav et al., 2014; Malecek and Poldrack, 2013), and must be incorporated into the final account of effort. Similarly, the concepts of cognitive dissonance and effort-justification from behavioral psychology and attempts to further demonstrate or refute effort-based boosting of value prove present key challenges for the unification of this literature. For example, future studies should examine the role of effort production upon modulation of risk taking or impulsivity, with particular emphasis upon the timing of action and outcome. Phasic dopamine release in striatum during effortful action may enhance the value of cues present during exertion, which may result in bias for those cues in subsequent free choice contexts. Similarly, neurophysiological studies have found neurons within cingulate cortex, amygdala and striatum that respond to modulation of effort and risk. Together, these results suggest there remains considerable opportunity to redefine key concepts and fundamental understanding of domain motivated behavior with new descriptive models and neural data.

5.6 Conclusion

5.6.1 Towards a Unified Account of Choice Behavior

Effort-based decision making comprises a fundamental aspect of animal behavior. The experiments presented in this thesis detailed aspects of how effort-based valuation affects choice behavior and neural activity. I demonstrated that the prospective effort paradigm improves upon previous attempts to test effort-based valuation and suggest the recruitment of distinct neural regions for effort-based valuation separated from production or anticipation of outcomes. I presented the results of our experiments in the context of previous human and animal studies of value-based decision making, and suggest new directions towards a unified account of choice behavior. Incorporation of ethologically valid tasks across mutliple levels of analysis to test model-driven predictions of effort's influence upon behavior and neural activity offers great promise to inform models of healthy cognition. Given the great societal cost of common impairments in motivated behavior, such models offer great promise to inform the next generation of behavioral and neurological treatments.

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